

What Is Claimed Is:

1. Use of an antibody drug conjugate (ADC) comprising an antibody or antigen binding fragment thereof conjugated to one or more units of a cytotoxic agent via a linker in the manufacture of a medicament for treating cancer in a subject in need thereof, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining region 1 (CDR-H1), CDR-H2, and CDR-H3 comprising the amino acid sequences of the corresponding CDR-H1, CDR-H2, and CDR-H3 in the heavy chain variable region sequence set forth in SEQ ID NO: 22 and a light chain variable region comprising CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of the corresponding CDR-L1, CDR-L2, and CDR-L3 in the light chain variable region sequence set forth in SEQ ID NO: 23, and wherein the antibody or antigen binding fragment thereof is conjugated to 1 to 20 units of MMAE via a linker;

wherein:

(1) the ADC is to be administered to the subject,

(2) an increase of expression of one or more ADC Set I Marker genes in the subject is determined, and

(3) (a) the ADC is continued to be administered to the subject if the expression of the one or more ADC Set I Marker genes in the subject is increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC, or

(b) the ADC is discontinued to be administered to the subject if the expression of the one or more ADC Set I Marker genes in the subject is not increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC;

wherein the one or more ADC Set I Marker genes comprise one or more major histocompatibility complex (MHC) signature genes, one or more toll-like receptor (TLR) family genes, one or more interleukin receptor family genes, one or more immune checkpoint receptor genes, one or more receptor tyrosine kinase genes, one or more IFN receptor family genes, one or more TNF family receptor genes, one or more inhibitory immunoreceptor genes, and/or one or more metabolic enzyme genes.

2. Use of an ADC comprising an antibody or antigen binding fragment thereof conjugated to one or more units of a cytotoxic agent via a linker in the manufacture of a medicament for treating cancer in a subject in need thereof, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining region 1 (CDR-H1), CDR-H2, and CDR-H3 comprising the amino acid sequences of the corresponding CDR-H1, CDR-H2, and CDR-H3 in the heavy chain variable region sequence set forth in SEQ ID NO: 22 and a light chain variable region comprising CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of the corresponding CDR-L1, CDR-L2, and CDR-L3 in the light chain variable region sequence set forth in SEQ ID NO: 23, and wherein the antibody or antigen binding fragment thereof is conjugated to 1 to 20 units of MMAE via a linker;

wherein:

- (1) a first dose of the ADC is to be administered to the subject,
- (2) an increase of expression of one or more ADC Set I Marker genes in the subject is determined, and
- (3) (a) a second dose of the ADC at the same or lower amount than the first dose is to be administered to the subject if the expression of the one or more ADC Set I Marker genes in the subject is increased compared to the expression of the one or more ADC Set I Marker genes

in the subject before the administration of the ADC, or

(b) a second dose of the ADC at a higher amount than the first dose is to be administered to the subject if the expression of the one or more ADC Set I Marker genes in the subject is not increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC;

wherein the one or more ADC Set I Marker genes comprise one or more MHC signature genes, one or more TLR family genes, one or more interleukin receptor family genes, one or more immune checkpoint receptor genes, one or more receptor tyrosine kinase genes, one or more IFN receptor family genes, one or more TNF family receptor genes, one or more inhibitory immunoreceptor genes, and/or one or more metabolic enzyme genes.

3. Use of an ADC comprising an antibody or antigen binding fragment thereof conjugated to one or more units of a cytotoxic agent via a linker in the manufacture of a medicament for treating cancer in a subject in need thereof, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining region 1 (CDR-H1), CDR-H2, and CDR-H3 comprising the amino acid sequences of the corresponding CDR-H1, CDR-H2, and CDR-H3 in the heavy chain variable region sequence set forth in SEQ ID NO: 22 and a light chain variable region comprising CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of the corresponding CDR-L1, CDR-L2, and CDR-L3 in the light chain variable region sequence set forth in SEQ ID NO: 23, and wherein the antibody or antigen binding fragment thereof is conjugated to 1 to 20 units of MMAE via a linker;

wherein:

(1) a first dose of the ADC is to be administered to the subject,

(2) an increase of expression of one or more ADC Set I Marker genes in the subject is determined, and

(3) (a) a second dose of the ADC is to be administered to the subject in conjunction with an immune checkpoint inhibitor if the expression of the one or more ADC Set I Marker genes in the subject is increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC, or

(b) a second dose of the ADC is to be administered to the subject without the immune checkpoint inhibitor if the expression of the one or more ADC Set I Marker genes in the subject is not increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC;

wherein the one or more ADC Set I Marker genes comprise one or more MHC signature genes, one or more TLR family genes, one or more interleukin receptor family genes, one or more immune checkpoint receptor genes, one or more receptor tyrosine kinase genes, one or more IFN receptor family genes, one or more TNF family receptor genes, one or more inhibitory immunoreceptor genes, and/or one or more metabolic enzyme genes.

4. Use of an ADC comprising an antibody or antigen binding fragment thereof conjugated to one or more units of a cytotoxic agent via a linker in the manufacture of a medicament for treating cancer in a subject in need thereof, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining region 1 (CDR-H1), CDR-H2, and CDR-H3 comprising the amino acid sequences of the corresponding CDR-H1, CDR-H2, and CDR-H3 in the heavy chain variable region sequence set forth in SEQ ID NO: 22 and a light chain variable region comprising CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of the corresponding CDR-L1, CDR-L2, and CDR-L3 in the light chain variable region sequence set forth in SEQ ID NO: 23, and wherein the antibody or antigen binding fragment thereof is conjugated to 1 to 20 units of MMAE via a linker;

wherein:

- (1) a first dose of the ADC is to be administered to the subject,
- (2) an increase of expression of one or more ADC Set I Marker genes in the subject is determined, and
- (3)
 - (a) the first dose of the ADC is to be administered to the subject with an immune checkpoint inhibitor if the expression of the one or more ADC Set I Marker genes in the subject is increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC, or
 - (b) a second dose of the ADC is to be administered to the subject without the immune checkpoint inhibitor if the expression of the one or more ADC Set I Marker genes in the subject is not increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC;

wherein the first dose of the ADC in (3)(a) is not to be administered to the subject in conjunction with the checkpoint inhibitor;

wherein the one or more ADC Set I Marker genes comprise one or more MHC signature genes, one or more TLR family genes, one or more interleukin receptor family genes, one or more immune checkpoint receptor genes, one or more receptor tyrosine kinase genes, one or more IFN receptor family genes, one or more TNF family receptor genes, one or more inhibitory immunoreceptor genes, and/or one or more metabolic enzyme genes.

5. Use of an ADC comprising an antibody or antigen binding fragment thereof conjugated to one or more units of a cytotoxic agent via a linker in the manufacture of a medicament for inducing immunogenic cell death (ICD) in a cancer in a subject in need thereof, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining region 1 (CDR-H1), CDR-H2, and CDR-H3

comprising the amino acid sequences of the corresponding CDR-H1, CDR-H2, and CDR-H3 in the heavy chain variable region sequence set forth in SEQ ID NO: 22 and a light chain variable region comprising CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of the corresponding CDR-L1, CDR-L2, and CDR-L3 in the light chain variable region sequence set forth in SEQ ID NO: 23, and wherein the antibody or antigen binding fragment thereof is conjugated to 1 to 20 units of MMAE via a linker;

wherein:

- (1) the ADC is to be administered to the subject,
- (2) an increase of expression of one or more ADC Set I Marker genes in the subject is determined, and
- (3)
 - (a) the ADC is continued to be administered to the subject if the expression of the one or more ADC Set I Marker genes in the subject is increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC, or
 - (b) the ADC is discontinued to be administered to the subject if the expression of the one or more ADC Set I Marker genes in the subject is not increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC;

wherein the one or more ADC Set I Marker genes comprise one or more MHC signature genes, one or more TLR family genes, one or more interleukin receptor family genes, one or more immune checkpoint receptor genes, one or more receptor tyrosine kinase genes, one or more IFN receptor family genes, one or more TNF family receptor genes, one or more inhibitory immunoreceptor genes, and/or one or more metabolic enzyme genes.

6. Use of an ADC comprising an antibody or antigen binding fragment thereof conjugated to one or more units of a cytotoxic agent via a linker in the manufacture of a

medicament for inducing ICD in a cancer in a subject in need thereof, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining region 1 (CDR-H1), CDR-H2, and CDR-H3 comprising the amino acid sequences of the corresponding CDR-H1, CDR-H2, and CDR-H3 in the heavy chain variable region sequence set forth in SEQ ID NO: 22 and a light chain variable region comprising CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of the corresponding CDR-L1, CDR-L2, and CDR-L3 in the light chain variable region sequence set forth in SEQ ID NO: 23, and wherein the antibody or antigen binding fragment thereof is conjugated to 1 to 20 units of MMAE via a linker;

wherein:

- (1) a first dose of the ADC is to be administered to the subject,
- (2) an increase of expression of one or more ADC Set I Marker genes in the subject is determined, and
- (3)
 - (a) a second dose of the ADC at the same or lower amount than the first dose is to be administered to the subject if the expression of the one or more ADC Set I Marker genes in the subject is increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC, or
 - (b) a second dose of the ADC at a higher amount than the first dose is to be administered to the subject if the expression of the one or more ADC Set I Marker genes in the subject is not increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC;

wherein the one or more ADC Set I Marker genes comprise one or more MHC signature genes, one or more TLR family genes, one or more interleukin receptor family genes, one or more immune checkpoint receptor genes, one or more receptor tyrosine kinase genes, one or

more IFN receptor family genes, one or more TNF family receptor genes, one or more inhibitory immunoreceptor genes, and/or one or more metabolic enzyme genes.

7. Use of an ADC comprising an antibody or antigen binding fragment thereof conjugated to one or more units of a cytotoxic agent via a linker in the manufacture of a medicament for inducing ICD in a cancer in a subject in need thereof, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining region 1 (CDR-H1), CDR-H2, and CDR-H3 comprising the amino acid sequences of the corresponding CDR-H1, CDR-H2, and CDR-H3 in the heavy chain variable region sequence set forth in SEQ ID NO: 22 and a light chain variable region comprising CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of the corresponding CDR-L1, CDR-L2, and CDR-L3 in the light chain variable region sequence set forth in SEQ ID NO: 23, and wherein the antibody or antigen binding fragment thereof is conjugated to 1 to 20 units of MMAE via a linker;

wherein:

- (1) a first dose of the ADC is to be administered to the subject,
- (2) an increase of expression of one or more ADC Set I Marker genes in the subject is determined, and
- (3)
 - (a) a second dose of the ADC is to be administered to the subject in conjunction with an immune checkpoint inhibitor if the expression of the one or more ADC Set I Marker genes in the subject is increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC, or
 - (b) a second dose of the ADC is to be administered to the subject without the immune checkpoint inhibitor if the expression of the one or more ADC Set I Marker genes in the

subject is not increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC;

wherein the one or more ADC Set I Marker genes comprise one or more MHC signature genes, one or more TLR family genes, one or more interleukin receptor family genes, one or more immune checkpoint receptor genes, one or more receptor tyrosine kinase genes, one or more IFN receptor family genes, one or more TNF family receptor genes, one or more inhibitory immunoreceptor genes, and/or one or more metabolic enzyme genes.

8. Use of an ADC comprising an antibody or antigen binding fragment thereof conjugated to one or more units of a cytotoxic agent via a linker in the manufacture of a medicament for inducing ICD in a cancer in a subject in need thereof, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining region 1 (CDR-H1), CDR-H2, and CDR-H3 comprising the amino acid sequences of the corresponding CDR-H1, CDR-H2, and CDR-H3 in the heavy chain variable region sequence set forth in SEQ ID NO: 22 and a light chain variable region comprising CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of the corresponding CDR-L1, CDR-L2, and CDR-L3 in the light chain variable region sequence set forth in SEQ ID NO: 23, and wherein the antibody or antigen binding fragment thereof is conjugated to 1 to 20 units of MMAE via a linker;

wherein:

- (1) a first dose of the ADC is to be administered to the subject,
- (2) an increase of expression of one or more ADC Set I Marker genes in the subject is determined, and
- (3) (a) the first dose of the ADC is to be administered to the subject with an immune checkpoint inhibitor if the expression of the one or more ADC Set I Marker genes in the subject

is increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC, or

(b) a second dose of the ADC is to be administered to the subject without the immune checkpoint inhibitor if the expression of the one or more ADC Set I Marker genes in the subject is not increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC;

wherein the first dose of the ADC in (3)(a) is not to be administered to the subject in conjunction with the checkpoint inhibitor;

wherein the one or more ADC Set I Marker genes comprise one or more MHC signature genes, one or more TLR family genes, one or more interleukin receptor family genes, one or more immune checkpoint receptor genes, one or more receptor tyrosine kinase genes, one or more IFN receptor family genes, one or more TNF family receptor genes, one or more inhibitory immunoreceptor genes, and/or one or more metabolic enzyme genes.

9. Use of an ADC comprising an antibody or antigen binding fragment thereof conjugated to one or more units of a cytotoxic agent via a linker in the manufacture of a medicament for inducing immune cell migration to a cancer in a subject in need thereof, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining region 1 (CDR-H1), CDR-H2, and CDR-H3 comprising the amino acid sequences of the corresponding CDR-H1, CDR-H2, and CDR-H3 in the heavy chain variable region sequence set forth in SEQ ID NO: 22 and a light chain variable region comprising CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of the corresponding CDR-L1, CDR-L2, and CDR-L3 in the light chain variable region sequence set forth in SEQ ID NO: 23, and wherein the antibody or antigen binding fragment thereof is conjugated to 1 to 20 units of MMAE via a linker;

wherein:

- (1) the ADC is to be administered to the subject,
- (2) an increase of expression of one or more ADC Set I Marker genes in the subject is determined, and
- (3)
 - (a) the ADC is continued to be administered to the subject if the expression of the one or more ADC Set I Marker genes in the subject is increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC, or
 - (b) the ADC is discontinued to be administered to the subject if the expression of the one or more ADC Set I Marker genes in the subject is not increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC;

wherein the one or more ADC Set I Marker genes comprise one or more MHC signature genes, one or more TLR family genes, one or more interleukin receptor family genes, one or more immune checkpoint receptor genes, one or more receptor tyrosine kinase genes, one or more IFN receptor family genes, one or more TNF family receptor genes, one or more inhibitory immunoreceptor genes, and/or one or more metabolic enzyme genes.

10. Use of an ADC comprising an antibody or antigen binding fragment thereof conjugated to one or more units of a cytotoxic agent via a linker in the manufacture of a medicament for inducing immune cell migration to a cancer in a subject in need thereof, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining region 1 (CDR-H1), CDR-H2, and CDR-H3 comprising the amino acid sequences of the corresponding CDR-H1, CDR-H2, and CDR-H3 in the heavy chain variable region sequence set forth in SEQ ID NO: 22 and a light chain variable region comprising CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of the corresponding CDR-L1, CDR-L2, and CDR-L3 in the light chain variable region sequence set

forth in SEQ ID NO: 23, and wherein the antibody or antigen binding fragment thereof is conjugated to 1 to 20 units of MMAE via a linker;

wherein:

- (1) a first dose of the ADC is to be administered to the subject,
- (2) an increase of expression of one or more ADC Set I Marker genes in the subject is determined, and
- (3)
 - (a) a second dose of the ADC at the same or lower amount than the first dose is to be administered to the subject if the expression of the one or more ADC Set I Marker genes in the subject is increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC, or
 - (b) a second dose of the ADC at a higher amount than the first dose is to be administered to the subject if the expression of the one or more ADC Set I Marker genes in the subject is not increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC;

wherein the one or more ADC Set I Marker genes comprise one or more MHC signature genes, one or more TLR family genes, one or more interleukin receptor family genes, one or more immune checkpoint receptor genes, one or more receptor tyrosine kinase genes, one or more IFN receptor family genes, one or more TNF family receptor genes, one or more inhibitory immunoreceptor genes, and/or one or more metabolic enzyme genes.

11. Use of an ADC comprising an antibody or antigen binding fragment thereof conjugated to one or more units of a cytotoxic agent via a linker in the manufacture of a medicament for inducing immune cell migration to a cancer in a subject in need thereof, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining region 1 (CDR-H1), CDR-H2, and CDR-H3

comprising the amino acid sequences of the corresponding CDR-H1, CDR-H2, and CDR-H3 in the heavy chain variable region sequence set forth in SEQ ID NO: 22 and a light chain variable region comprising CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of the corresponding CDR-L1, CDR-L2, and CDR-L3 in the light chain variable region sequence set forth in SEQ ID NO: 23, and wherein the antibody or antigen binding fragment thereof is conjugated to 1 to 20 units of MMAE via a linker;

wherein:

- (1) a first dose of the ADC is to be administered to the subject,
- (2) an increase of expression of one or more ADC Set I Marker genes in the subject is determined, and
- (3)
 - (a) a second dose of the ADC is to be administered to the subject in conjunction with an immune checkpoint inhibitor if the expression of the one or more ADC Set I Marker genes in the subject is increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC, or
 - (b) a second dose of the ADC is to be administered to the subject without the immune checkpoint inhibitor if the expression of the one or more ADC Set I Marker genes in the subject is not increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC;

wherein the one or more ADC Set I Marker genes comprise one or more MHC signature genes, one or more TLR family genes, one or more interleukin receptor family genes, one or more immune checkpoint receptor genes, one or more receptor tyrosine kinase genes, one or more IFN receptor family genes, one or more TNF family receptor genes, one or more inhibitory immunoreceptor genes, and/or one or more metabolic enzyme genes.

12. Use of an ADC comprising an antibody or antigen binding fragment thereof conjugated to one or more units of a cytotoxic agent via a linker in the manufacture of a medicament for inducing immune cell migration to a cancer in a subject in need thereof, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining region 1 (CDR-H1), CDR-H2, and CDR-H3 comprising the amino acid sequences of the corresponding CDR-H1, CDR-H2, and CDR-H3 in the heavy chain variable region sequence set forth in SEQ ID NO: 22 and a light chain variable region comprising CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of the corresponding CDR-L1, CDR-L2, and CDR-L3 in the light chain variable region sequence set forth in SEQ ID NO: 23, and wherein the antibody or antigen binding fragment thereof is conjugated to 1 to 20 units of MMAE via a linker;

wherein:

- (1) a first dose of the ADC is to be administered to the subject,
- (2) an increase of expression of one or more ADC Set I Marker genes in the subject is determined, and
- (3)
 - (a) the first dose of the ADC is to be administered to the subject with an immune checkpoint inhibitor if the expression of the one or more ADC Set I Marker genes in the subject is increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC, or
 - (b) a second dose of the ADC is to be administered to the subject without the immune checkpoint inhibitor if the expression of the one or more ADC Set I Marker genes in the subject is not increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC;

wherein the ADC in (3)(a) is not to be administered in conjunction with the checkpoint inhibitor;

wherein the one or more ADC Set I Marker genes comprise one or more MHC signature genes, one or more TLR family genes, one or more interleukin receptor family genes, one or more immune checkpoint receptor genes, one or more receptor tyrosine kinase genes, one or more IFN receptor family genes, one or more TNF family receptor genes, one or more inhibitory immunoreceptor genes, and/or one or more metabolic enzyme genes.

13. Use of an ADC comprising an antibody or antigen binding fragment thereof conjugated to one or more units of a cytotoxic agent via a linker in the manufacture of a medicament for increasing expression of one or more ADC Set I Marker genes in a cancer in a subject in need thereof, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining region 1 (CDR-H1), CDR-H2, and CDR-H3 comprising the amino acid sequences of the corresponding CDR-H1, CDR-H2, and CDR-H3 in the heavy chain variable region sequence set forth in SEQ ID NO: 22 and a light chain variable region comprising CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of the corresponding CDR-L1, CDR-L2, and CDR-L3 in the light chain variable region sequence set forth in SEQ ID NO: 23, and wherein the antibody or antigen binding fragment thereof is conjugated to 1 to 20 units of MMAE via a linker;

wherein:

(1) the ADC is to be administered to the subject,

(2) an increase of the expression of the one or more ADC Set I Marker genes in the subject is determined, and

(3) (a) the ADC is continued to be administered to the subject if the expression of the one or more ADC Set I Marker genes in the subject is increased compared to the expression of

the one or more ADC Set I Marker genes in the subject before the administration of the ADC, or

(b) the ADC is discontinued to be administered to the subject if the expression of the one or more ADC Set I Marker genes in the subject is not increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC;

wherein the one or more ADC Set I Marker genes comprise one or more MHC signature genes, one or more TLR family genes, one or more interleukin receptor family genes, one or more immune checkpoint receptor genes, one or more receptor tyrosine kinase genes, one or more IFN receptor family genes, one or more TNF family receptor genes, one or more inhibitory immunoreceptor genes, and/or one or more metabolic enzyme genes.

14. Use of an ADC comprising an antibody or antigen binding fragment thereof conjugated to one or more units of a cytotoxic agent via a linker in the manufacture of a medicament for increasing expression of one or more ADC Set I Marker genes in a cancer in a subject in need thereof, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining region 1 (CDR-H1), CDR-H2, and CDR-H3 comprising the amino acid sequences of the corresponding CDR-H1, CDR-H2, and CDR-H3 in the heavy chain variable region sequence set forth in SEQ ID NO: 22 and a light chain variable region comprising CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of the corresponding CDR-L1, CDR-L2, and CDR-L3 in the light chain variable region sequence set forth in SEQ ID NO: 23, and wherein the antibody or antigen binding fragment thereof is conjugated to 1 to 20 units of MMAE via a linker;

wherein:

(1) a first dose of the ADC is to be administered to the subject,

(2) an increase of the expression of the one or more ADC Set I Marker genes in the subject is determined, and

(3) (a) a second dose of the ADC at the same or lower amount than the first dose is to be administered to the subject if the expression of the one or more ADC Set I Marker genes in the subject is increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC, or

(b) a second dose of the ADC at a higher amount than the first dose is to be administered to the subject if the expression of the one or more ADC Set I Marker genes in the subject is not increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC;

wherein the one or more ADC Set I Marker genes comprise one or more MHC signature genes, one or more TLR family genes, one or more interleukin receptor family genes, one or more immune checkpoint receptor genes, one or more receptor tyrosine kinase genes, one or more IFN receptor family genes, one or more TNF family receptor genes, one or more inhibitory immunoreceptor genes, and/or one or more metabolic enzyme genes.

15. Use of an ADC comprising an antibody or antigen binding fragment thereof conjugated to one or more units of a cytotoxic agent via a linker in the manufacture of a medicament for increasing expression of one or more ADC Set I Marker genes in a cancer in a subject in need thereof, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining region 1 (CDR-H1), CDR-H2, and CDR-H3 comprising the amino acid sequences of the corresponding CDR-H1, CDR-H2, and CDR-H3 in the heavy chain variable region sequence set forth in SEQ ID NO: 22 and a light chain variable region comprising CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of the corresponding CDR-L1, CDR-L2, and CDR-L3 in the light chain variable region sequence set forth in SEQ ID NO: 23, and wherein the antibody or antigen binding fragment thereof is conjugated to 1 to 20 units of MMAE via a linker;

wherein:

- (1) a first dose of the ADC is to be administered to the subject,
- (2) an increase of the expression of the one or more ADC Set I Marker genes in the subject is determined, and
- (3)
 - (a) a second dose of the ADC is to be administered to the subject in conjunction with an immune checkpoint inhibitor if the expression of the one or more ADC Set I Marker genes in the subject is increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC, or
 - (b) a second dose of the ADC is to be administered to the subject without the immune checkpoint inhibitor if the expression of the one or more ADC Set I Marker genes in the subject is not increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC;

wherein the one or more ADC Set I Marker genes comprise one or more MHC signature genes, one or more TLR family genes, one or more interleukin receptor family genes, one or more immune checkpoint receptor genes, one or more receptor tyrosine kinase genes, one or more IFN receptor family genes, one or more TNF family receptor genes, one or more inhibitory immunoreceptor genes, and/or one or more metabolic enzyme genes.

16. Use of an ADC comprising an antibody or antigen binding fragment thereof conjugated to one or more units of a cytotoxic agent via a linker in the manufacture of a medicament for increasing expression of one or more ADC Set I Marker genes in a cancer in a subject in need thereof, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining region 1 (CDR-H1), CDR-H2, and CDR-H3 comprising the amino acid sequences of the corresponding CDR-H1, CDR-H2, and CDR-H3 in the heavy chain variable region sequence set forth in SEQ ID NO: 22 and a light

chain variable region comprising CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences of the corresponding CDR-L1, CDR-L2, and CDR-L3 in the light chain variable region sequence set forth in SEQ ID NO: 23, and wherein the antibody or antigen binding fragment thereof is conjugated to 1 to 20 units of MMAE via a linker;

wherein:

(1) a first dose of the ADC is to be administered to the subject,

(2) an increase of the expression of the one or more ADC Set I Marker genes in the subject is determined, and

(3) (a) the first dose of the ADC is to be administered to the subject with an immune checkpoint inhibitor if the expression of the one or more ADC Set I Marker genes in the subject is increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC, or

(b) a second dose of the ADC is to be administered to the subject without the immune checkpoint inhibitor if the expression of the one or more ADC Set I Marker genes in the subject is not increased compared to the expression of the one or more ADC Set I Marker genes in the subject before the administration of the ADC;

wherein the ADC in (3)(a) is not to be administered in conjunction with the checkpoint inhibitor;

wherein the one or more ADC Set I Marker genes comprise one or more MHC signature genes, one or more TLR family genes, one or more interleukin receptor family genes, one or more immune checkpoint receptor genes, one or more receptor tyrosine kinase genes, one or more IFN receptor family genes, one or more TNF family receptor genes, one or more inhibitory immunoreceptor genes, and/or one or more metabolic enzyme genes.

17. The use of any one of claims 1 to 16, wherein the antibody or antigen binding fragment thereof is an anti-nectin-4 antibody or antigen binding fragment thereof.

18. The use of any one of claims 1 to 17, wherein the one or more ADC Set I Marker genes comprise one or more MHC signature genes.

19. The use of any one of claims 1 to 18, wherein the one or more MHC signature genes comprise one or more MHC class genes, wherein the one or more MHC signature genes comprise:

(i) one or more MHC class I genes, wherein the one or more MHC class I genes comprise one or more genes selected from the group consisting of human leukocyte antigens-A (HLA-A), HLA-B, HLA-C, HLA-E, HLA-F, and Transporter 2, ATP binding cassette subfamily B member (TAP2); or

(ii) one or more MHC class II genes, wherein the one or more MHC class II genes comprise one or more genes selected from the group consisting of HLA-DMA, HLA-DMB, HLA-DRB1, HLA-DRA, and HLA-DPA1.

20. The use of claim 19, wherein: (i) the one or more MHC class genes or the one or more MHC class II genes do not comprise HLA-DPB1; or (ii) the MHC signature gene, the MHC class gene, or the MHC class II gene is not HLA-DPB1.

21. The use of claims 19 or 20, wherein the one or more MHC class genes comprise one or more MHC class III genes, wherein the one or more MHC class III genes comprise one or more genes selected from the group consisting of LST1, LTB, AIF1, and TNF.

22. The use of any one of claims 1 to 21, wherein the one or more MHC signature genes comprise one or more MHC regulator genes, wherein the one or more MHC regulator genes comprise one or more genes selected from the group consisting of interferon regulatory

factor (IRF) genes, nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) family genes, signal transducer and activator of transcription (STAT) family genes, CTCF, CIITA, RFX transcription factor family genes, SPI1, and nuclear transcription factor Y (NFY) genes.

23. The use of claim 22, wherein:

(i) the NF-κB family genes comprise one or more genes selected from the group consisting of nuclear factor kappa B subunit 1 (NFKB1), NFKB2, RELA, RELB, and REL;

(ii) the NF-κB family genes comprise NFKB2, RELA, or both NFKB2 and RELA;

(iii) the STAT family genes comprise one or more genes selected from the group consisting of STAT1, STAT2, STAT3, STAT4, STAT5, and STAT6;

(iv) the STAT family gene is STAT2;

(v) the RFX transcription factor family genes comprise one or more genes selected from the group consisting of RFX1, RFX5, RFX7, RFXAP and RFXANK;

(vi) the IRF genes comprise IRF7, IRF8, or both IRF7 and IRF8; and/or

(vii) the NFY genes comprise NFYA, NFYC, or both NFYA and NFYC.

24. The use of claim 22 or 23, wherein the one or more MHC regulator genes comprise CTCF, CIITA, and/or SPI1.

25. The use of any one of claims 1 to 24, wherein the one or more ADC Set I Marker genes comprise:

(i) one or more TLR family genes, wherein the one or more TLR family genes comprise one or more genes selected from the group consisting of TLR9, TLR8, and TLR7, further wherein the one or more TLR family genes do not comprise TLR3; or

(ii) one or more interleukin receptor family genes, wherein the one or more interleukin receptor family genes comprise one or more genes selected from the group consisting of IL2RA, IL2RB, IL2RG, IL21R, IL27R, IL1RN, IL17RA, IL3RA, IL1R1, IL17RC, IL20RA, and IL22RA1, further wherein the one or more interleukin receptor family genes comprise IL2RA.

26. The use of any one of claims 1 to 25, wherein the one or more ADC Set I Marker genes comprise one or more immune checkpoint receptor genes, wherein one or more immune checkpoint receptor genes comprise one or more B7 family genes, one or more Ig superfamily genes, or both one or more B7 family genes and one or more Ig superfamily genes, further wherein:

(i) the B7 family genes comprise VTCN1, CD276, or both VTCN1 and CD276;

(ii) the Ig superfamily genes comprise (a) nectin family genes or (b) nectin family genes and LAG3, wherein the nectin family genes comprise one or more genes selected from the group consisting of PVRIG, PVRL2, and TIGIT; or

(iii) the Ig superfamily genes comprise LAG3.

27. The use of any one of claims 1 to 26, wherein the one or more ADC Set I Marker genes comprise one or more receptor tyrosine kinase genes, wherein:

(i) the receptor tyrosine kinase genes comprise one or more genes selected from the group consisting of CSF1R, PDGFRB, TEK/TIE2, and FLT3; or

(ii) the receptor tyrosine kinase genes comprise CSF1R.

28. The use of any one of claims 1 to 27, wherein the one or more ADC Set I Marker genes comprise one or more TNF family receptor genes, wherein the TNF family receptor genes comprise one or more genes selected from the group consisting of CD40, TNFRSF1A, TNFRSF21, and TNFRSF1B.

29. The use of any one of claims 1 to 28, wherein the one or more ADC Set I Marker genes comprise one or more IFN receptor family genes, wherein:

(i) the IFN receptor family genes comprise IFNAR1, IFNAR2, or both IFNAR1 and IFNAR2; or

(ii) the IFN receptor family genes comprise IFNAR1.

30. The use of any one of claims 1 to 29, wherein the one or more ADC Set I Marker genes comprise one or more inhibitory immunoreceptor genes, wherein:

(i) the inhibitory immunoreceptor genes comprise TIM3, VSIR, or both TIM3 and VSIR;

(ii) the inhibitory immunoreceptor genes comprise VSIR; or

(iv) the inhibitory immunoreceptor genes comprise TIM3.

31. The use of any one of claims 1 to 30, wherein the one or more ADC Set I Marker genes comprise one or more metabolic enzyme genes, wherein:

(i) the metabolic enzyme genes comprise one or more genes selected from the group consisting of indoleamine 2,3-dioxygenase 1 (IDO1), TDO2, EIF2AK2, ACSS1, and ACSS2; or

(ii) the metabolic enzyme genes comprise IDO1.

32. The use of any one of claims 1 to 31, wherein the use further comprises determining an increase of expression of one or more ADC Set II Marker genes in the subject

compared to the expression of the one or more ADC Set II Marker genes in the subject before the administration of the ADC in step (1), wherein the administration in step (3)(a) is further conditioned on the increase of the expression of the one or more ADC Set II Marker genes.

33. The use of claim 32, wherein the one or more ADC Set II Marker genes comprise one or more genes selected from the group consisting of ER stress genes, ER/mitochondria ATPase genes, cell death genes, T cell stimulator genes, macrophage/innate immunity stimulator genes, chemoattractant genes, Rho GTPase genes, Rho GTPase regulator genes, mitotic arrest genes, siglec family genes, GO positive autophagy regulator genes, and GTPase related kinase genes, wherein:

(i) the ER stress genes comprise one or more genes selected from the group consisting of XBP-1S, ERP29, TRAF2, c-JUN, BCL2L11, BCAP31, SERINC3, DAP2IP, ERN1, ATF6, NCK2, PPP1R15A, UBQLN2, BAG6, and BOK;

(ii) the ER stress genes do not comprise EDEM2 or XBP-1L;

(iii) the ER/mitochondria ATPase genes comprise one or more genes selected from the group consisting of ATP2A3, MT-ATP6, and MT-ATP8;

(iv) the cell death genes comprise one or more genes selected from the group consisting of Bax, BCL2L1, BCL2L11, and BOK;

(v) the cell death genes do not comprise FAS;

(vi) the T cell stimulator genes comprise MIG (CXCL9), IP10 (CXCL10), or both MIG and IP10;

(vii) the macrophage/innate immunity stimulator genes comprise IL-1 α , M-CSF (CSF), or both IL-1 α and M-CSF;

(viii) the chemoattractant genes comprise one or more genes selected from the group consisting of Eotaxin (CCL11), MIP1 α , MIP1 β , and MCP1;

(ix) the Rho GTPase genes comprise one or more genes selected from the group consisting of RhoB, RhoF, and RhoG;

(x) the Rho GTPase genes do not comprise any one of CDC42, RhoA, and RhoC;

(xi) the Rho GTPase regulator genes comprise one or more genes selected from the group consisting of DAP2IP, ARHGEF18, ARHGEF5, and RASAL1;

(xii) the mitotic arrest genes comprise one or more genes selected from the group consisting of CCND1, CDKN1A, GADD45B, E4F1, CDC14B, and DAPK1;

(xiii) the mitotic arrest genes do not comprise DDIAS or CDK1;

(xiv) the siglec family genes comprise siglec1;

(xv) the GO positive autophagy regulator genes comprise one or more genes selected from the group consisting of BCL2L11, ROCK1, TSC1, TSC2, BAG3, MFN2, RIPK1, RIPK4, HDAC6, STK11, ULK1, FOXO1, FOXO3, and MUL1;

(xvi) the GO positive autophagy regulator genes do not comprise BNIP3 or BNIP3L;
and/or

(xvii) the GTPase related kinase genes comprise ROCK1, PAK4, or both ROCK1 and PAK4.

34. The use of any one of claims 1 to 33, wherein the increase in any of the gene expression is an increase of:

(i) 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, 110%, 120%, 130%, 140%, 150%, 160%, 170%, 180%, 190%, 200%, 250%, 300%, 350%, 400%, 450%, 500%, 550%, 600%, 650%, 700%, 750%, 800%, 850%, 900%, 950%, 1000%, or more; or

(ii) 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30 fold or more.

35. The use of any one of claims 3, 4, 7, 8, 11, 12, and 15 to 34, wherein the immune checkpoint inhibitor is a PD-1 inhibitor, a PD-L1 inhibitor, a PD-L2 inhibitor, a CTLA-4 inhibitor, a LAG-3 inhibitor, a B7 inhibitor, a TIM3 (HAVCR2) inhibitor, an OX40 (CD134) inhibitor, a GITR agonist, a CD137 agonist, a CD40 agonist, a VTCN1 inhibitor, an IDO1 inhibitor, a CD276 inhibitor, a PVRIG inhibitor, a TIGIT inhibitor, a CD25 (IL2RA) inhibitor, an IFNAR2 inhibitor, an IFNAR1 inhibitor, a CSF1R inhibitor, a VSIR (VISTA) inhibitor, or an therapeutic agent targeting HLA.

36. The use of any one of claims 3, 4, 7, 8, 11, 12, and 15 to 35, wherein the immune checkpoint inhibitor is:

(i) an anti-PD-1 antibody, wherein the anti-PD-1 antibody is BGB-A317, nivolumab, pembrolizumab, cemiplimab, CT-011, camrelizumab, sintilimab, tislelizumab, TSR-042, PDR001, or toripalimab;

(ii) an anti-PD-L1 antibody, wherein the anti-PD-L1 antibody is durvalumab, BMS-936559, atezolizumab, MEDI4736, or avelumab;

(iii) an anti-PD-L2 antibody, wherein the anti-PD-L2 antibody is rHlgM12B7A;

(iv) a VTCN1 inhibitor, wherein the VTCN1 inhibitor is FPA150;

(v) an IDO1 inhibitor, wherein the IDO1 inhibitor is Epacadostat, BMS986205, Navoximod, PF-06840003, KHK2455, RG70099, IOM-E, or IOM-D;

(vi) a TIGIT inhibitor, wherein the a TIGIT inhibitor is MTIG7192A, BMS-986207, OMP-313M32, MK-7684, AB154, CGEN-15137, SEA-TIGIT, ASP8374, or AJUD008;

(vii) a VSIR inhibitor, wherein the VSIR inhibitor is CA-170, JNJ 61610588, or HMBD-002;

(viii) a TIM3 inhibitor, wherein the TIM3 inhibitor is AJUD009;

(ix) a CD25 (IL2RA) inhibitor, wherein the CD25 (IL2RA) inhibitor is daclizumab or basiliximab;

(x) an IFNAR1 inhibitor, wherein the IFNAR1 inhibitor is anifrolumab or sifalimumab;

(xi) a CSF1R inhibitor, wherein the CSF1R inhibitor is pexidartinib, emactuzumab, cabiralizumab, ARRY-382, BLZ945, AJUD010, AMG820, IMC-CS4, JNJ-40346527, PLX5622, or FPA008; or

(xii) a therapeutic agent targeting HLA, wherein the therapeutic agent targeting HLA is GSK01, IMC-C103C, IMC-F106C, IMC-G107C, or ABBV-184.

37. The use of any one of claims 1 to 36, wherein the antibody or antigen binding fragment thereof comprises CDR-H1 comprising the amino acid sequence of SEQ ID NO:9, CDR-H2 comprising the amino acid sequence of SEQ ID NO:10, CDR-H3 comprising the amino acid sequence of SEQ ID NO:11; CDR-L1 comprising the amino acid sequence of SEQ ID NO:12, CDR-L2 comprising the amino acid sequence of SEQ ID NO:13, and CDR-L3 comprising the amino acid sequence of SEQ ID NO:14, or

wherein the antibody or antigen binding fragment thereof comprises CDR-H1 comprising the amino acid sequence of SEQ ID NO:16, CDR-H2 comprising the amino acid sequence of SEQ ID NO:17, CDR-H3 comprising the amino acid sequence of SEQ ID NO:18; CDR-L1 comprising the amino acid sequence of SEQ ID NO:19, CDR-L2 comprising the amino acid

sequence of SEQ ID NO:20, and CDR-L3 comprising the amino acid sequence of SEQ ID NO:21.

38. The use of any one of claims 1 to 37, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:22 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:23.

39. The use of any one of claims 1 to 38, wherein the antibody comprises a heavy chain comprising the amino acid sequence ranging from the 20th amino acid (glutamic acid) to the 466th amino acid (lysine) of SEQ ID NO:7 and a light chain comprising the amino acid sequence ranging from the 23rd amino acid (aspartic acid) to the 236th amino acid (cysteine) of SEQ ID NO:8.

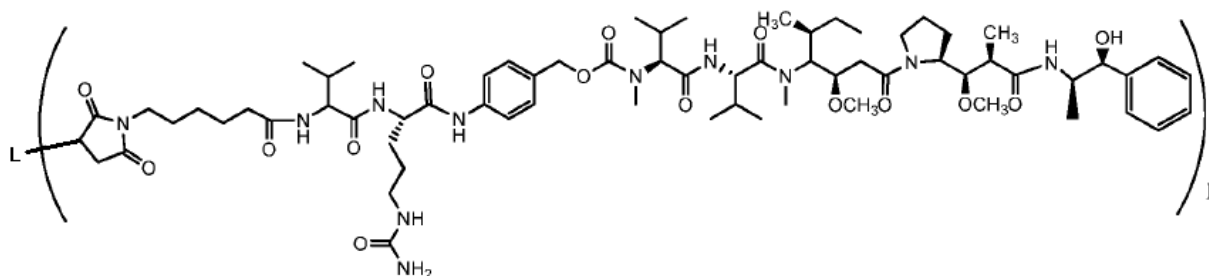
40. The use of any one of claims 1 to 39, wherein:

(i) the antigen binding fragment is an Fab, F(ab')₂, Fv or scFv, wherein the antigen binding fragment thereof is recombinantly produced;

(ii) the antibody is a fully human antibody, wherein the antibody thereof is recombinantly produced; or

(iii) the antibody or antigen binding fragment thereof is recombinantly produced.

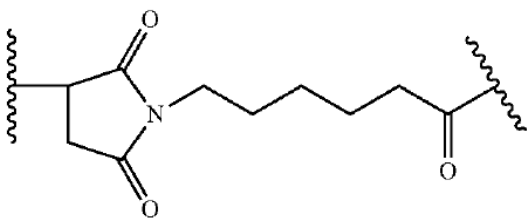
41. The use of any one of claims 1 to 40, wherein the ADC has the following structure:



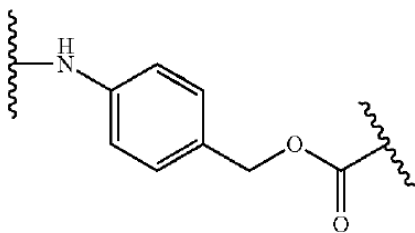
wherein L- represents the antibody or antigen binding fragment thereof and p is from 1 to 10, from 2 to 8, or from 3 to 5.

42. The use of any one of claims 1 to 40, wherein the antibody or antigen binding fragment is conjugated to each unit of MMAE via a linker, wherein the linker is an enzyme-cleavable linker, and wherein the linker forms a bond with a sulfur atom of the antibody or antigen binding fragment thereof; further wherein the linker has a formula of: $-Aa-Ww-Yy-$, wherein $-A-$ is a stretcher unit, a is 0 or 1; $-W-$ is an amino acid unit, w is an integer ranging from 0 to 12; and $-Y-$ is a spacer unit, y is 0, 1, or 2; further wherein the stretcher unit forms a bond with a sulfur atom of the antibody or antigen binding fragment thereof; and wherein the spacer unit is linked to MMAE via a carbamate group.

43. The use of claim 42, wherein the stretcher unit has the structure of Formula (1) below; the amino acid unit is valine-citrulline; and the spacer unit is a PAB group comprising the structure of Formula (2) below:



Formula (1)



Formula (2).

44. The use of any one of claims 1 to 40, 42, and 43, wherein the ADC comprises:

- (i) from 1 to 20 units of MMAE per antibody or antigen binding fragment thereof;
- (ii) from 1 to 10 units of MMAE per antibody or antigen binding fragment thereof;
- (iii) from 2 to 8 units of MMAE per antibody or antigen binding fragment thereof; or
- (iv) from 3 to 5 units of MMAE per antibody or antigen binding fragment thereof.

45. The use of any one of claims 1, 5, 9, 13, and 17 to 44, wherein:

(i) the ADC is to be administered at a dose of 1 to 10 mg/kg of the subject's body weight, 1 to 5 mg/kg of the subject's body weight, 1 to 2.5 mg/kg of the subject's body weight, or 1 to 1.25 mg/kg of the subject's body weight;

(ii) the ADC is to be administered at a dose of about 0.25 mg/kg, about 0.5 mg/kg, about 0.75 mg/kg, about 1.0 mg/kg, about 1.25 mg/kg, about 1.5 mg/kg, about 1.75 mg/kg, about 2.0 mg/kg, about 2.25 mg/kg, or about 2.5 mg/kg of the subject's body weight;

(iii) the ADC is to be administered at a dose of about 1 mg/kg of the subject's body weight; or

(iv) the ADC is to be administered at a dose of about 1.25 mg/kg of the subject's body weight.

46. The use of any one of claims 2 to 4, 6 to 8, 10 to 12, 14 to 44, wherein the first dose of the ADC is a dose of:

(i) 1 to 10 mg/kg of the subject's body weight, 1 to 5 mg/kg of the subject's body weight, 1 to 2.5 mg/kg of the subject's body weight, or 1 to 1.25 mg/kg of the subject's body weight;

(ii) about 0.5 mg/kg, about 0.75 mg/kg, about 1.0 mg/kg, about 1.25 mg/kg, about 1.5 mg/kg, about 1.75 mg/kg, about 2.0 mg/kg, about 2.25 mg/kg, or about 2.5 mg/kg of the subject's body weight;

(iii) about 1 mg/kg of the subject's body weight; or

(iv) about 1.25 mg/kg of the subject's body weight.

47. The use of claim 46, wherein the second dose of the ADC is:

(i) lower than the first dose by 0.1 mg/kg to 1 mg/kg of the subject's body weight;

(ii) lower than the first dose by about 0.1 mg/kg, about 0.2 mg/kg, about 0.25 mg/kg, about 0.3 mg/kg, about 0.4 mg/kg, about 0.5 mg/kg, about 0.6 mg/kg, about 0.7 mg/kg, about 0.75 mg/kg, about 0.8 mg/kg, about 0.9 mg/kg, or about 1 mg/kg of the subject's body weight;

(iii) lower than the first dose by about 0.25 mg/kg of the subject's body weight;

(iv) lower than the first dose by about 0.5 mg/kg of the subject's body weight; or

(v) lower than the first dose by about 0.75 mg/kg of the subject's body weight.

48. The use of claim 46 or 47, wherein the second dose of the ADC is:

(i) lower than the first dose by about 1.0 mg/kg of the subject's body weight;

(ii) a dose of about 0.25 mg/kg, about 0.5 mg/kg, about 0.75 mg/kg, about 1.0 mg/kg, about 1.25 mg/kg, about 1.5 mg/kg, about 1.75 mg/kg, about 2.0 mg/kg, or about 2.25 mg/kg of the subject's body weight; or

(iii) identical to the first dose of the ADC.

49. The use of any one of claims 1 to 48, wherein the ADC is to be administered by:

(i) an intravenous (IV) injection or infusion;

(ii) an IV injection or infusion three times every four-week cycle;

(iii) an IV injection or infusion on Days 1, 8 and 15 of every four-week cycle;

(iv) an IV injection or infusion over about 30 minutes three times every four-week cycle;

or

(v) an IV injection or infusion over about 30 minutes on Days 1, 8 and 15 of every four-week cycle.

50. The use of any one of claims 1 to 49, wherein the ADC is formulated in a pharmaceutical composition comprising:

(i) L-histidine, polysorbate-20, and trehalose dihydrate;

(ii) the ADC is formulated in a pharmaceutical composition comprising about 20 mM L-histidine, about 0.02% (w/v) polysorbate-20, about 5.5% (w/v) trehalose dihydrate, and hydrochloride, and wherein the pH of the pharmaceutical composition is about 6.0 at 25°C; or

(iii) the ADC is formulated in a pharmaceutical composition comprising about 9 mM histidine, about 11 mM histidine hydrochloride monohydrate, about 0.02% (w/v) polysorbate-20, and about 5.5% (w/v) trehalose dihydrate, and wherein the pH of the pharmaceutical composition is about 6.0 at 25°C.

51. The use of any one of claims 1 to 50, wherein the cancer is bladder cancer, urothelial cancer, gastric cancer, esophageal cancer, head and neck cancer, squamous non-small cell lung cancer (NSCLC), non-squamous NSCLC, breast cancer, ovarian cancer, cervical cancer, biliary cancer and cholangiocarcinomas, pancreatic cancer, squamous cell carcinoma of the vulva and penis, prostate adenocarcinoma, or endometrial carcinoma.

52. The use of any one of claims 1 to 51, wherein the cancer is locally advanced cancer or metastatic cancer.

53. The use of claim 51 or 52, wherein the breast cancer is ER negative, PR negative, and HER2 negative (ER-/PR-/HER2-) breast cancer.

54. The use of any one of claims 51 to 53, wherein the breast cancer is hormone receptor positive and human epidermal growth factor receptor 2 negative (HR+/HER2-) breast cancer.

55. The use of claim 51 or 52, wherein the urothelial cancer is papillary urothelial carcinoma or flat urothelial carcinoma.

56. The use of claim 51 or 52, wherein the bladder cancer is non-muscle-invasive bladder cancer (NMIBC) or muscle-invasive bladder cancer, wherein the muscle-invasive bladder cancer is squamous cell carcinoma, adenocarcinoma, small cell carcinoma, or sarcoma.