

ANTIBODY-DRUG CONJUGATE METABOLITES

[0001] This application claims the benefit of U.S. Provisional Application No. 63/590,288, filed on October 13, 2023, the contents of which are incorporated by reference in their entirety.

[0002] The present disclosure relates to methods of analysis of antibody-drug conjugates (ADCs), e.g., those comprising eribulin, and the quantitative assessment of intact ADC or metabolites thereof *in vitro* and *in vivo*. Antibodies and antigen-binding fragments thereof suitable for use in the assays are also disclosed.

BACKGROUND

[0003] When analyzing ADCs, for example to provide quantitative assessment of ADC concentration and metabolism *in vitro* or *in vivo*, the typical assays performed involve assessing total antibody (both conjugated and unconjugated antibody), intact ADC (all conjugated antibody species with drug-to-antibody ratio (DAR) > 0, generally measured in a DAR-insensitive manner), and free payload. Assessment of total antibody and intact ADC are almost exclusively determined using immunoassay methods, while free payload is typically measured by quantitative mass spectrometry. While providing valuable information on components of ADC metabolism, these assays often do not provide a complete picture of the overall metabolic process. Intact ADC assays are typically DAR-insensitive, i.e., all DAR species are recovered equally, which simplifies the interpretation of pharmacokinetic analyses by reducing the complexity of test agent to a single species – conjugated antibody. However, intact ADC assays can overrepresent ADC stability, especially for ADCs with higher starting DAR (e.g., DAR4 to DAR8 or higher). These ADCs could lose all but one of their conjugated payloads or linker-payloads to chemical or enzymatic processes and still be quantitated in the intact ADC assay as “intact.” Furthermore, other biologically active payload-containing metabolites could be generated in the process of ADC metabolism, and these would not be captured solely with a free payload assay. Thus, a need remains for improved ADC analytical assays.

[0004] One option for improved assays could comprise immunological methods. The measurement of intact ADC by immunological methods, however, requires the use of specific immunoreagents (typically antibodies or antigen-binding fragments) that recognize either the payload alone or the linker-payload, wherein the epitope is comprised of components of both

the linker and payload. Antibodies that recognize the payload alone have the added benefit that they can be used in assays to quantify ADC properties where the payload is paired with many different linker structures, making them useful in early-stage conjugate research activities where the final linker-payload structure is not fixed. Payload-recognizing agents with desirable features of high affinity and specificity for the payload alone may have broader utility beyond use in intact ADC assays, such as in immunodepletion of ADCs, immunopurification of conjugated species, and immunohistochemical analyses of ADCs in tissues.

[0005] Maleimide-based ADCs can undergo a process in matrix and in circulation known as retro-Michael deconjugation, where the intact maleimide linker-payload is released. Maleimides are highly reactive, have very short half-lives in plasma, and have several potential metabolic fates (FIG. 1). In some instances, these linker-payload species may represent the majority of payload-related metabolites in circulation. These metabolites are typically measured using mass spectrometry. However, the quantitative assessment of these species by mass spectrometry represents an analytical challenge because each linker-payload metabolite has a unique mass and thus requires a separate assay. Furthermore, protein conjugate metabolites, such as albumin conjugates, would not be amenable to mass spectrometry methods for quantitation. It would therefore be beneficial to have a method to quantitate additional metabolites or all non-antibody conjugated linker-payload metabolites in total.

[0006] Accordingly, in various embodiments, the present disclosure provides improved methods and reagents for detecting and quantifying intact antibody-drug conjugates, constituent antibody-drug conjugate parts such as a linker-payload, e.g., Mal-(PEG)₂-VCP-eribulin, and metabolites in a biological sample.

SUMMARY

[0007] In various embodiments, the present disclosure provides, in part, a method for detecting a metabolite of an antibody-drug conjugate, wherein the metabolite is a linker-payload and the payload moiety is eribulin. In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered the antibody-drug conjugate. In some embodiments, the method comprises contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to an

antibody portion of the antibody-drug conjugate and/or an unconjugated antibody or antigen-binding fragment. In some embodiments, the method comprises contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to the payload moiety of the linker-payload. In some embodiments, the method comprises contacting the biological sample with a third antibody or antigen-binding fragment, wherein the third antibody or antigen-binding fragment is capable of specifically binding to the linker of the linker-payload. In some embodiments, the method comprises detecting a signal from the third antibody or antigen-binding fragment. In some embodiments, the metabolite in the biological sample is detected.

[0008] In various embodiments, the present disclosure provides a method for detecting a metabolite of an antibody-drug conjugate, wherein the metabolite is a linker-payload and the payload moiety is eribulin. In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered the antibody-drug conjugate. In some embodiments, the method comprises contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the antibody-drug conjugate and/or an unconjugated antibody or antigen-binding fragment. In some embodiments, the method comprises contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to the payload moiety of the linker-payload. In some embodiments, the method comprises contacting the biological sample with a third antibody or antigen-binding fragment, wherein the third antibody or antigen-binding fragment is capable of specifically binding to albumin. In some embodiments, the method comprises detecting a signal from the third antibody or antigen-binding fragment. In some embodiments, the metabolite in the biological sample is detected.

[0009] In some embodiments, contacting of the biological sample with the first antibody immunodepletes intact antibody-drug conjugate from the biological sample.

[0010] In some embodiments, the first antibody or antigen-binding fragment specifically binds farletuzumab or a fragment thereof. In some embodiments, the first antibody or antigen-binding fragment specifically binds 345A12-HC15-LC4 or a fragment thereof. In some embodiments, the first antibody or antigen-binding fragment is an anti-human IgG Fc antibody or antigen-binding fragment thereof. In some embodiments, the linker-payload comprises Val-Cit-pAb-eribulin ("VCP-eribulin"). In some embodiments, the linker-payload

comprises Mal-(PEG)₂-VCP-eribulin. In some embodiments, the third antibody or antigen-binding fragment specifically binds Val-Cit-pAB ("VCP").

[0011] In various embodiments, the present disclosure provides a method for detecting a metabolite of an antibody-drug conjugate, wherein the metabolite is a linker-payload comprising Val-Cit-pAB-eribulin ("VCP-eribulin") and the payload moiety is eribulin, wherein the antibody-drug conjugate is MORAb-202. In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered MORAb-202. In some embodiments, the method comprises contacting the biological sample with 2G9. In some embodiments, the method comprises contacting the biological sample with 5E4. In some embodiments, the method comprises contacting the biological sample with 11G6. In some embodiments, the method comprises detecting a signal from 11G6. In some embodiments, the metabolite in the biological sample is detected.

[0012] In various embodiments, the present disclosure provides a method for detecting a metabolite of an antibody-drug conjugate, wherein the metabolite is a linker-payload comprising Val-Cit-pAB-eribulin ("VCP-eribulin") and the payload moiety is eribulin, wherein the antibody-drug conjugate is MORAb-202. In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered MORAb-202. In some embodiments, the method comprises contacting the biological sample with 2G9. In some embodiments, the method comprises contacting the biological sample with 5E4. In some embodiments, the method comprises contacting the biological sample with an anti-albumin antibody. In some embodiments, the method comprises detecting a signal from the anti-albumin antibody. In some embodiments, the metabolite in the biological sample is detected.

[0013] In various embodiments, the present disclosure provides a method for detecting a metabolite of an antibody-drug conjugate, wherein the metabolite is a linker-payload comprising Val-Cit-pAB-eribulin ("VCP-eribulin") and the payload moiety is eribulin, wherein the antibody-drug conjugate is MORAb-109. In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered MORAb-109. In some embodiments, the method comprises contacting the biological sample with a first antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment comprises an anti-human IgG Fc or an anti-idiotypic antibody or antigen binding fragment. In some embodiments, the anti-idiotypic antibody or antigen-binding fragment

comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286. In some embodiments, the method comprises contacting the biological sample with 5E4. In some embodiments, the method comprises contacting the biological sample with 11G6. In some embodiments, the method comprises detecting a signal from 11G6. In some embodiments, the metabolite in the biological sample is detected.

[0014] In various embodiments, the present disclosure provides a method for detecting a metabolite of an antibody-drug conjugate, wherein the metabolite is a linker-payload comprising Val-Cit-pAB-eribulin (“VCP-eribulin”) and the payload moiety is eribulin, wherein the antibody-drug conjugate is MORAb-109. In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered MORAb-109. In some embodiments, the method comprises contacting the biological sample with a first antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment comprises an anti-human IgG Fc or an anti-idiotypic antibody or antigen binding fragment. In some embodiments, the anti-idiotypic antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286. In some embodiments, the method comprises contacting the biological sample with 5E4. In some embodiments, the method comprises contacting the biological sample with an anti-albumin antibody. In some embodiments, the method comprises detecting a signal from the anti-albumin antibody. In some embodiments, the metabolite in the biological sample is detected.

[0015] In various embodiments, the present disclosure provides a method for detecting total antibody-drug conjugate (ADC) and/or unconjugated antibody or antigen-binding fragment, wherein the ADC is MORAb-202 and the unconjugated antibody or antigen-binding fragment is farletuzumab or an antigen-binding fragment thereof. In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered MORAb-202. In some embodiments, the method comprises contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC and/or an unconjugated antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment is an anti-idiotypic antibody. In some embodiments, the anti-idiotypic antibody specifically binds farletuzumab or a fragment

thereof. In some embodiments, the method comprises contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to a second epitope of the antibody portion of the ADC and/or the unconjugated antibody or antigen-binding fragment, wherein the second antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment. In some embodiments, the method comprises detecting a signal from the second antibody or antigen-binding fragment. In some embodiments, the total ADC and/or unconjugated antibody or antigen-binding fragment in the biological sample is detected.

[0016] In various embodiments, the present disclosure provides a method for detecting total antibody-drug conjugate (ADC) and/or unconjugated antibody or antigen-binding fragment, wherein the ADC is MORAb-202 and the unconjugated antibody or antigen-binding fragment is farletuzumab or an antigen-binding fragment thereof. In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered MORAb-202. In some embodiments, the method comprises contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC and/or the unconjugated antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment. In some embodiments, the method comprises contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to a second epitope of the antibody portion of the ADC and/or the unconjugated antibody or antigen-binding fragment, wherein the second antibody or antigen-binding fragment is an anti-idiotypic antibody. In some embodiments, the anti-idiotypic antibody specifically binds farletuzumab or a fragment thereof. In some embodiments, the method comprises detecting a signal from the second antibody or antigen-binding fragment. In some embodiments, the total ADC and/or unconjugated antibody or antigen-binding fragment in the biological sample is detected.

[0017] In various embodiments, the present disclosure provides a method for detecting total antibody-drug conjugate (ADC) and/or unconjugated antibody or antigen-binding fragment, wherein the ADC is MORAb-109 and the unconjugated antibody or antigen-binding fragment is 345A12-HC15-LC4 or an antigen-binding fragment thereof. In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered MORAb-109. In some embodiments, the method comprises contacting the

biological sample with a first antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC and/or the unconjugated antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment is an anti-idiotypic antibody. In some embodiments, the anti-idiotypic antibody specifically binds 345A12-HC15-LC4 or a fragment thereof. In some embodiments, the method comprises contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to a second epitope of the antibody portion of the ADC and/or the unconjugated antibody or antigen-binding fragment, wherein the second antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment. In some embodiments, the method comprises detecting a signal from the second antibody or antigen-binding fragment. In some embodiments, the total ADC and/or unconjugated antibody or antigen-binding fragment in the biological sample is detected.

[0018] In various embodiments, the present disclosure provides a method for detecting total antibody-drug conjugate (ADC) and/or unconjugated antibody or antigen-binding fragment, wherein the ADC is MORAb-109 and the unconjugated antibody or antigen-binding fragment is 345A12-HC15-LC4 or an antigen-binding fragment thereof. In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered MORAb-109. In some embodiments, the method comprises contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC and/or the unconjugated antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment. In some embodiments, the method comprises contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to a second epitope of the antibody portion of the ADC and/or the unconjugated antibody or antigen-binding fragment, wherein the second antibody or antigen-binding fragment is an anti-idiotypic antibody. In some embodiments, the anti-idiotypic antibody specifically binds 345A12-HC15-LC4 or a fragment thereof. In some embodiments, the method comprises detecting a signal from the second antibody or antigen-binding fragment. In some embodiments, the total ADC and/or unconjugated antibody or antigen-binding fragment in the biological sample is detected.

[0019] In various embodiments, the present disclosure provides a method for detecting total antibody-drug conjugate (ADC) and/or unconjugated antibody or antigen-binding fragment,

wherein the ADC is MORAb-202 and the unconjugated antibody or antigen-binding fragment is farletuzumab or an antigen-binding fragment thereof. In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered MORAb-202. In some embodiments, the method comprises contacting the biological sample with a first antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment comprises 2G9. In some embodiments, the method comprises contacting the biological sample with a second antibody or antigen-binding fragment, wherein the second antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment. In some embodiments, the method comprises detecting a signal from second antibody or antigen-binding fragment. In some embodiments, the total ADC and/or unconjugated antibody or antigen-binding fragment in the biological sample is detected.

[0020] In various embodiments, the present disclosure provides a method for detecting total antibody-drug conjugate (ADC) and/or unconjugated antibody or antigen-binding fragment, wherein the ADC is MORAb-202 and the unconjugated antibody or antigen-binding fragment is farletuzumab or an antigen-binding fragment thereof. In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered MORAb-202. In some embodiments, the method comprises contacting the biological sample with a first antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment. In some embodiments, the method comprises contacting the biological sample with a second antibody or antigen-binding fragment, wherein the second antibody or antigen-binding fragment comprises 2G9. In some embodiments, the method comprises detecting a signal from the second antibody or antigen-binding fragment. In some embodiments, the total ADC and/or unconjugated antibody or antigen-binding fragment in the biological sample is detected.

[0021] In various embodiments, the present disclosure provides a method for detecting total antibody-drug conjugate (ADC) and/or unconjugated antibody or antigen-binding fragment, wherein the ADC is MORAb-109 and the unconjugated antibody or antigen-binding fragment is 345A12-HC15-LC4 or an antigen-binding fragment thereof. In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered MORAb-109. In some embodiments, the method comprises contacting the

biological sample with a first antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286. In some embodiments, the method comprises contacting the biological sample with a second antibody or antigen-binding fragment, wherein the second antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment. In some embodiments, the method comprises detecting a signal from second antibody or antigen-binding fragment. In some embodiments, the total ADC and/or unconjugated antibody or antigen-binding fragment in the biological sample is detected.

[0022] In various embodiments, the present disclosure provides a method for detecting total antibody-drug conjugate (ADC) and/or unconjugated antibody or antigen-binding fragment, wherein the ADC is MORAb-109 and the unconjugated antibody or antigen-binding fragment is 345A12-HC15-LC4 or an antigen-binding fragment thereof. In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered MORAb-109. In some embodiments, the method comprises contacting the biological sample with a first antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment. In some embodiments, the method comprises contacting the biological sample with a second antibody or antigen-binding fragment, wherein the second antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286. In some embodiments, the method comprises detecting a signal from the second antibody or antigen-binding fragment. In some embodiments, the total ADC and/or unconjugated antibody or antigen-binding fragment in the biological sample is detected.

[0023] In various embodiments, the present disclosure provides a method for detecting intact antibody-drug conjugate (ADC), wherein the ADC is MORAb-202. In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered MORAb-202. In some embodiments, the method comprises contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to eribulin. In some embodiments, the method comprises contacting the biological

sample with a second antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC, wherein the second antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment or an anti-idiotypic antibody or antigen-binding fragment. In some embodiments, the anti-idiotypic antibody specifically binds farletuzumab or a fragment thereof. In some embodiments, the method comprises detecting a signal from the second antibody or antigen-binding fragment. In some embodiments, the intact ADC in the biological sample is detected.

[0024] In various embodiments, the present disclosure provides a method for detecting intact antibody-drug conjugate (ADC), wherein the ADC is MORAb-202. In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered MORAb-202. In some embodiments, the method comprises contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC and/or an antigen-binding fragment thereof, wherein the first antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment or an anti-idiotypic antibody or antigen-binding fragment. In some embodiments, the anti-idiotypic antibody specifically binds farletuzumab or a fragment thereof. In some embodiments, the method comprises contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to eribulin. In some embodiments, the method comprises detecting a signal from the second antibody or antigen-binding fragment. In some embodiments, the intact ADC in the biological sample is detected.

[0025] In various embodiments, the present disclosure provides a method for detecting intact antibody-drug conjugate (ADC), wherein the ADC is MORAb-109. In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered MORAb-109. In some embodiments, the method comprises contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to eribulin. In some embodiments, the method comprises contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC, wherein the second antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment or an anti-idiotypic antibody or antigen-binding fragment. In some embodiments, the anti-idiotypic antibody specifically binds 345A12-HC15-LC4 or a fragment thereof. In some embodiments, the

method comprises detecting a signal from the second antibody or antigen-binding fragment.

In some embodiments, the intact ADC in the biological sample is detected.

[0026] In various embodiments, the present disclosure provides a method for detecting intact antibody-drug conjugate (ADC), wherein the ADC is MORAb-109. In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered MORAb-109. In some embodiments, the method comprises contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC, wherein the first antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment or an anti-idiotypic antibody or antigen-binding fragment. In some embodiments, the anti-idiotypic antibody specifically binds 345A12-HC15-LC4 or a fragment thereof. In some embodiments, the method comprises contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to eribulin. In some embodiments, the method comprises detecting a signal from the second antibody or antigen-binding fragment. In some embodiments, the intact ADC in the biological sample is detected.

[0027] In various embodiments, the present disclosure provides a method for detecting intact antibody-drug conjugate (ADC), wherein the ADC is MORAb-202. In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered MORAb-202. In some embodiments, the method comprises contacting the biological sample with a first antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment is 5E4. In some embodiments, the method comprises contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC, wherein the second antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment or is 2G9 or an antigen-binding fragment thereof. In some embodiments, the method comprises detecting a signal from the second antibody or antigen-binding fragment. In some embodiments, the intact ADC in the biological sample is detected.

[0028] In various embodiments, the present disclosure provides a method for detecting intact antibody-drug conjugate (ADC), wherein the ADC is MORAb-202. In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered MORAb-202. In some embodiments, the method comprises contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically

binding to an antibody portion of the ADC and/or an antigen-binding fragment thereof, wherein the first antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment, or is 2G9 or an antigen-binding fragment. In some embodiments, the method comprises contacting the biological sample with a second antibody or antigen-binding, wherein the second antibody or antigen-binding fragment is 5E4. In some embodiments, the method comprises detecting a signal from the second antibody or antigen-binding fragment. In some embodiments, the intact ADC in the biological sample is detected.

[0029] In various embodiments, the present disclosure provides a method for detecting intact antibody-drug conjugate (ADC), wherein the ADC is MORAb-109. In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered MORAb-109. In some embodiments, the method comprises contacting the biological sample with a first antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment is 5E4. In some embodiments, the method comprises contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC, wherein the second antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment or an anti-idiotypic antibody or antigen-binding fragment. In some embodiments, the anti-idiotypic antibody comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286. In some embodiments, the method comprises detecting a signal from the second antibody or antigen-binding fragment. In some embodiments, the intact ADC in the biological sample is detected.

[0030] In various embodiments, the present disclosure provides a method for detecting intact antibody-drug conjugate (ADC), wherein the ADC is MORAb-109. In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered MORAb-109. In some embodiments, the method comprises contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC and/or an antigen-binding fragment thereof, wherein the first antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment or an anti-idiotypic antibody or antigen binding fragment. In some embodiments, the anti-idiotypic antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:

285, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286. In some embodiments, the method comprises contacting the biological sample with a second antibody or antigen-binding, wherein the second antibody or antigen-binding fragment is 5E4. In some embodiments, the method comprises detecting a signal from the second antibody or antigen-binding fragment. In some embodiments, the intact ADC in the biological sample is detected.

[0031] In various embodiments, the present disclosure provides a method for detecting intact and/or total antibody-drug conjugate (ADC) and/or a metabolite of an ADC, wherein the metabolite is unconjugated antibody or antigen-binding fragment, linker-payload, and/or free payload.

[0032] In various embodiments, the present disclosure provides an antibody or antigen-binding fragment thereof capable of binding to an antibody-drug conjugate comprising farletuzumab and/or to farletuzumab or an antigen-binding fragment thereof. In some embodiments, the antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 13, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 14.

[0033] In some embodiments, the antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 1 (HCDR1), SEQ ID NO: 2 (HCDR2), and SEQ ID NO: 3 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 4 (LCDR1), SEQ ID NO: 5 (LCDR2), and SEQ ID NO: 6 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 7 (HCDR1), SEQ ID NO: 8 (HCDR2), and SEQ ID NO: 9 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 10 (LCDR1), SEQ ID NO: 11 (LCDR2), and SEQ ID NO: 12 (LCDR3), as defined by the IMGT numbering system.

[0034] In some embodiments, the antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 13, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 14.

[0035] In some embodiments, the antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 15, and a light chain comprising an amino acid sequence of SEQ ID NO: 16.

[0036] In various embodiments, the present disclosure provides an antibody or antigen-binding fragment thereof capable of binding to an antibody-drug conjugate comprising 345A12-HC15-LC4 and/or to 345A12-HC15-LC4 or an antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286.

[0037] In some embodiments, the antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 273 (HCDR1), SEQ ID NO: 274 (HCDR2), and SEQ ID NO: 275 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 276 (LCDR1), SEQ ID NO: 277 (LCDR2), and SEQ ID NO: 278 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 279 (HCDR1), SEQ ID NO: 280 (HCDR2), and SEQ ID NO: 281 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 282 (LCDR1), SEQ ID NO: 283 (LCDR2), and SEQ ID NO: 284 (LCDR3), as defined by the IMGT numbering system.

[0038] In some embodiments, the antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286.

[0039] In some embodiments, the antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 287, and a light chain comprising an amino acid sequence of SEQ ID NO: 288.

[0040] In various embodiments, the present disclosure provides an antibody or antigen-binding fragment thereof capable of binding to eribulin.

[0041] In some embodiments, the antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions from a heavy chain variable region

comprising an amino acid sequence of SEQ ID NO: 29, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 30.

[0042] In some embodiments, the antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions (HCDRs) comprising amino acid sequences of SEQ ID NO: 17 (HCDR1), SEQ ID NO: 18 (HCDR2), and SEQ ID NO: 19 (HCDR3); and three light chain complementarity determining regions (LCDRs) comprising amino acid sequences of SEQ ID NO: 20 (LCDR1), SEQ ID NO: 21 (LCDR2), and SEQ ID NO: 22 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 23 (HCDR1), SEQ ID NO: 24 (HCDR2), and SEQ ID NO: 25 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 26 (LCDR1), SEQ ID NO: 27 (LCDR2), and SEQ ID NO: 28 (LCDR3), as defined by the IMGT numbering system.

[0043] In some embodiments, the antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 29, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 30.

[0044] In some embodiments, the antibody or antigen-binding fragment is an antigen-binding fragment. In some embodiments, the antigen-binding fragment is a Fab fragment.

[0045] In some embodiments, the antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 31, and a light chain comprising an amino acid sequence of SEQ ID NO: 32.

[0046] In some embodiments, the antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 294, and a light chain comprising an amino acid sequence of SEQ ID NO: 32.

[0047] In some embodiments, the antibody or antigen-binding fragment is an anti-eribulin antibody or antigen-binding fragment disclosed herein, e.g., in Tables 16-19.

[0048] In various embodiments, the present disclosure provides an antibody or antigen-binding fragment thereof capable of binding to Val-Cit-pAB ("VCP").

[0049] In some embodiments, the antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 45, and three light chain

complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 46.

[0050] In some embodiments, the antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 33 (HCDR1), SEQ ID NO: 34 (HCDR2), and SEQ ID NO: 35 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 36 (LCDR1), SEQ ID NO: 37 (LCDR2), and SEQ ID NO: 38 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 39 (HCDR1), SEQ ID NO: 40 (HCDR2), and SEQ ID NO: 41 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 42 (LCDR1), SEQ ID NO: 43 (LCDR2), and SEQ ID NO: 38 (LCDR3), as defined by the IMGT numbering system.

[0051] In some embodiments, the antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 45, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 46.

[0052] In some embodiments, the antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 47, and a light chain comprising an amino acid sequence of SEQ ID NO: 48.

[0053] In some embodiments, the antibody or antigen-binding fragment is an anti-VCP antibody or antigen-binding fragment disclosed herein, e.g., in Tables 22-25.

[0054] In some embodiments, an antibody or antigen-binding fragment disclosed herein is conjugated to a label. In some embodiments, the label comprises a fluorescent tag, a luminescent tag, an electrochemiluminescent tag, an enzyme reporter, a biotin, or a bead. In some embodiments, the label is a biotin. In some embodiments, the label is a bead. In some embodiments, the bead is an agarose bead or a magnetic bead. In some embodiments, the label is a fluorescent tag.

BRIEF DESCRIPTION OF THE DRAWINGS

[0055] FIG. 1 provides various metabolic pathways for maleimide-based ADCs.

[0056] FIG. 2 shows forms of Mal-(PEG)₂-VCP-eribulin immunizing and screening reagents.

[0057] FIG. 3 shows titer of rabbit immunized with KLH-(Mal-(PEG)₂-VCP-eribulin) represented by bleed dilution factor (1/x).

[0058] FIG. 4 shows linker-payload structures and bio-layer interferometry (BLI) binding data used in screening anti-Mal-(PEG)₂-VCP-eribulin clones. The linker-payloads structures used in the screening of an initial 12-gene rescued clones are shown in FIG 4A. FIG. 4B shows BLI binding curves for the initial 12 gene-rescued clones. The VH and VL protein sequences for anti-Mal-(PEG)₂-VCP eribulin antibodies are shown in FIG. 4C. The linker payload structures of MORAb-003-based ADCs used to screen 6 selected clones are shown in FIG. 4D. BLI binding trace data for anti-Mal-(PEG)₂-VCP-eribulin antibodies binding to MORAb-003 and MORAb-003 ADCs are shown in FIG. 4E. FIG. 4F shows BLI binding curve data for 11G6 specificity.

[0059] FIG. 5 shows sensogram data for 5E4 binding affinity. The first column displays 5E4 binding affinity, the second columns shows AbD26976 binding affinity, and the third column shows AbD26978 binding affinity.

[0060] FIG. 6 is a schematic of an assay for measuring intact MORAb-202 using a biotinylated 5E4 monovalent Fab fragment as a capture reagent and anti-farletuzumab antibody 2G9 as a detector on the Gyros Xpand platform (FIG. 6A). FIG. 6B shows a standard binding curve.

[0061] FIG. 7 is a schematic of an assay for measuring intact MORAb-109 using biotinylated 5E4 monovalent Fab fragment as a capture reagent and an anti-human Fc (CH2-specific) antibody as a detector on the Gyros XPand platform (FIG. 7A). FIG. 7B shows a standard binding curve.

[0062] FIGS. 8A-B show the pharmacokinetics (PK) of MORAb-109 administered as an IV bolus dose in normal mice treated with MORAb-109 at a dose of either 10 mg/kg or 25 mg/kg. FIG. 8C shows DAR and percent maleimide hydrolysis of MORAb-109 in normal mice.

[0063] FIGS. 9A-C show MORAb-109 PK in NCI-H2110 tumor-bearing mice at a dose of 25 mg/kg or 50 mg/kg in plasma (FIG. 9A) or tumor tissues (FIG. 9B), and the corresponding PK parameters (FIG. 9C).

[0064] FIGS. 10A-B show mean concentration of total antibody, intact ADC, or eribulin after administration of MORAb-109 in cynomolgus monkeys (IV bolus, 2 monkeys) (FIG.

10A), and corresponding DAR and percent maleimide hydrolysis after MORAb-109 administration (FIG. 10B).

[0065] FIGS. 11A-B show the concentration of MORAb-109 DAR2 and MORAb-109 DAR4 in plasma from normal rats dosed at 25 mg/kg or 75 mg/kg (FIG. 11A) and corresponding PK parameters (FIG. 11B).

[0066] FIG. 12 is a schematic of an assay measuring intact anti-trastuzumab using a biotinylated 5E4 monovalent Fab fragment as a capture reagent and anti-trastuzumab as a detector on the Gyros Xpand platform (FIG. 12A). FIG. 12B shows a standard binding curve.

[0067] FIG. 13 shows the stability of various trastuzumab-eribulin ADCs in both mouse plasma and human plasma (FIG. 13A). The structures of linker-payloads attached to antibodies via transglutaminase transamidation onto the amide nitrogen of the glutamine residue in each linker are shown in FIG. 13B in red. Corresponding PK parameters in normal mice injected with an IV bolus of either 5 mg/kg or 20 mg/kg of eribulin-conjugated trastuzumab are shown in FIGS. 13C-D.

[0068] FIG. 14 shows a schematic of an immunodepletion assay followed by linker-payload quantification (FIG. 14A) and dynamic range of quantification assay (FIG. 14B).

[0069] FIGS. 15A-C show free linker-payload from MORAb-109 DAR2 in mouse plasma (comparison with random conjugation) (FIG. 15A), DAR and percent maleimide hydrolysis of MORAb-109 (FIG. 15B), and free eribulin and Mal-(PEG)₂-VCP-eribulin in mouse plasma (FIG. 15C).

[0070] FIG. 16 shows released linker-payload and free payload after treatment with MORAb-109 in mouse or human plasma following maleimide ring opening.

[0071] FIG. 17 is a schematic of an assay for detecting eribulin-conjugated albumin species in plasma.

[0072] FIGS. 18A-C show the total released linker-payload, eribulin-conjugated albumin, and free eribulin in plasma from mice, humans, or monkeys treated with MORAb-202 (FIG. 18), percent DAR loss after MORAb-202 treatment (FIG. 18B), and percent maleimide hydrolysis after MORAb-202 treatment (FIG. 18C). FIG. 18D shows MORAb-202 plasma stability in monkeys.

[0073] FIG. 19 shows total antibody, intact ADC, total non-ADC linker-payload, eribulin-conjugated albumin, and free payload in MORAb-202-dosed non-human primate (NHP) (FIG. 19A) and PK parameters (FIG. 19B).

[0074] FIGS. 20A-B show levels of circulating total antibody, intact ADC, albumin-eribulin conjugate, and free eribulin (FIG. 20A) and corresponding PK parameters (FIG. 20B) in normal rats dosed with MORAb-109. FIG. 20C shows DAR loss due to retro-Michael release and maleimide hydrolysis in normal rats dosed with MORAb-109.

[0075] FIG. 21 shows staining of human ovarian cancer xenograft OVCAR-3 tumors from MORAb-202-treated mice.

[0076] FIG. 22 shows staining of human lung cancer xenograft NCI-H2110 tumors from MORAb-109-treated mice (day 3 post-treatment).

[0077] FIG. 23 shows an analytical workflow diagram.

DETAILED DESCRIPTION

[0078] The disclosed compositions and methods may be understood more readily by reference to the following detailed description taken in connection with the accompanying figures, which form a part of this disclosure. It is to be understood that the terminology used herein is for the purpose of describing particular embodiments by way of example only and is not intended to be limiting of the claimed compositions and methods unless the context indicates otherwise.

[0079] Throughout this text, the descriptions refer to compositions and methods of using the compositions. Where the disclosure describes or claims a feature or embodiment associated with a composition, such a feature or embodiment is equally applicable to the methods of using the composition. Likewise, where the disclosure describes or claims a feature or embodiment associated with a method of using a composition, such a feature or embodiment is equally applicable to the composition.

[0080] When a range of values is expressed, it includes embodiments using any particular value within the range. Further, reference to values stated in ranges includes each and every value within that range. All ranges are inclusive of their endpoints and combinable. When values are expressed as approximations, by use of the antecedent “about,” it will be understood that the particular value forms another embodiment. Reference to a particular numerical value includes at least that particular value unless the context clearly dictates otherwise. The use of “or” will mean “and/or” unless the specific context of its use dictates otherwise. All references cited herein are incorporated by reference for any purpose. Where a reference and the specification conflict, the specification will control.

[0081] It is to be appreciated that certain features of the disclosed compositions and methods, which are, for clarity, described herein in the context of separate embodiments, may also be provided in combination in a single embodiment. Conversely, various features of the disclosed compositions and methods that are, for brevity, described in the context of a single embodiment, may also be provided separately or in any subcombination.

Definitions

[0082] Various terms relating to aspects of the description are used throughout the specification and claims. Such terms are to be given their ordinary meaning in the art unless otherwise indicated. Other specifically defined terms are to be construed in a manner consistent with the definitions provided herein.

[0083] As used herein, the singular forms “a,” “an,” and “the” include plural forms unless the context clearly dictates otherwise.

[0084] The terms “about” or “approximately” in the context of numerical values and ranges refers to values or ranges that approximate or are close to the recited values or ranges such that the embodiment may perform as intended, such as having a desired amount of nucleic acids or polypeptides in a reaction mixture, as is apparent to the skilled person from the teachings contained herein. Thus, these terms encompass values beyond those resulting from systematic error. In some embodiments, about means plus or minus 10% of a numerical amount.

[0085] The terms “antibody-drug conjugate,” “antibody conjugate,” “conjugate,” “immunoconjugate,” and “ADC” are used interchangeably, and refer to a therapeutic compound (e.g., an eribulin moiety) that is linked to an antibody moiety and is defined by the generic formula: $Ab-(L-D)_p$ (Formula I), wherein Ab is an antibody moiety (e.g., an antibody or antigen-binding fragment), L is a linker moiety, D is a drug moiety (e.g., an eribulin drug moiety), and p is the number of drug moieties per antibody moiety. In ADCs comprising an eribulin drug moiety, “ p ” refers to the number of eribulin moieties linked to the antibody moiety. In some embodiments, the linker L can include a cleavable moiety that can either directly attach to the antibody moiety and to the therapeutic compound, or the cleavable moiety can be attached to either or both the antibody moiety and therapeutic compound by spacer unit(s). In some embodiments, when a spacer unit attaches the cleavable moiety to the therapeutic compound, it is a self-immolative spacer unit.

[0086] As used herein, “intact,” in the context of an ADC, refers to an ADC that remains attached to its original number of linker-payload moieties, e.g., if an ADC has DAR4, an “intact” ADC has an average ratio of 4 linker-payload moieties per antibody in solution, e.g., plasma.

[0087] The term “antibody” is used in the broadest sense to refer to an immunoglobulin molecule that recognizes and specifically binds to a target, such as a protein, polypeptide, carbohydrate, polynucleotide, lipid, or combinations of the foregoing through at least one antigen recognition site within the variable region of the immunoglobulin molecule. The heavy chain of an antibody is composed of a heavy chain variable domain (VH) and a heavy chain constant region (CH). The light chain is composed of a light chain variable domain (VL) and a light chain constant domain (CL). For the purposes of this application, the mature heavy chain and light chain variable domains each comprise three complementarity determining regions (CDR1, CDR2, and CDR3) within four framework regions (FR1, FR2, FR3, and FR4) arranged from N-terminus to C-terminus: FR1, CDR1, FR2, CDR2, FR3, CDR3, and FR4. An “antibody” can be naturally occurring or man-made, such as monoclonal antibodies produced by conventional hybridoma technology. The term “antibody” includes full-length monoclonal antibodies and full-length polyclonal antibodies, as well as antibody fragments such as Fab, Fab', F(ab')₂, Fv, and single chain antibodies. An antibody can be any one of the five major classes of immunoglobulins: IgA, IgD, IgE, IgG, and IgM, or subclasses thereof (e.g., isotypes IgG1, IgG2, IgG3, IgG4). The term further encompasses human antibodies, chimeric antibodies, humanized antibodies and any modified immunoglobulin molecule containing an antigen recognition site, so long as it demonstrates the desired biological activity.

[0088] The term “monoclonal antibody,” as used herein, refers to an antibody obtained from a population of substantially homogeneous antibodies, i.e., the individual antibodies comprising the population are identical except for possible naturally occurring mutations that may be present in minor amounts. Monoclonal antibodies are highly specific, being directed against a single antigenic epitope. In contrast, conventional (polyclonal) antibody preparations typically include a multitude of antibodies directed against (or specific for) different epitopes. The modifier “monoclonal” indicates the character of the antibody as being obtained from a substantially homogeneous population of antibodies, and is not to be construed as requiring production of the antibody by any particular method. For example, the

monoclonal antibodies to be used in accordance with the present disclosure may be made by the hybridoma method first described by Kohler et al. (1975) Nature 256:495, or may be made by recombinant DNA methods (see, e.g., U.S. Patent No. 4,816,567). Monoclonal antibodies may also be isolated from phage antibody libraries using the techniques described in Clackson et al. (1991) Nature 352:624-8, and Marks et al. (1991) J. Mol. Biol. 222:581-97, for example.

[0089] The monoclonal antibodies described herein specifically include “chimeric” antibodies, in which a portion of the heavy and/or light chain is identical with or homologous to corresponding sequences in antibodies derived from a particular species or belonging to a particular antibody class or subclass, while the remainder of the chain(s) is identical with or homologous to corresponding sequences in antibodies derived from another species or belonging to another antibody class or subclass, as well as fragments of such antibodies, so long as they specifically bind the target antigen and/or exhibit the desired biological activity.

[0090] The term “chimeric antibody,” as used herein, refers to antibodies wherein the amino acid sequence of the immunoglobulin molecule is derived from two or more species. In some instances, the variable regions of both heavy and light chains correspond to the variable regions of antibodies derived from one species with the desired specificity, affinity, and activity while the constant regions are homologous to antibodies derived from another species (e.g., human) to minimize an immune response in the latter species.

[0091] As used herein, the term “humanized antibody” refers to forms of antibodies that contain sequences from non-human (e.g., rabbit) antibodies as well as human antibodies. Such antibodies are chimeric antibodies which contain minimal sequences derived from non-human immunoglobulin. In general, the humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the hypervariable loops correspond to those of a non-human immunoglobulin and all or substantially all of the framework (FR) regions are those of a human immunoglobulin sequence. The humanized antibody optionally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin. The humanized antibody can be further modified by the substitution of residues, either in the Fv framework region and/or within the replaced non-human residues to refine and optimize antibody specificity, affinity, and/or activity.

[0092] The term “antigen-binding fragment,” “antigen-binding domain,” or “antigen-binding portion” of an antibody, as used herein, refers to one or more fragments of an antibody or protein that retain the ability to specifically bind to an antigen (e.g., eribulin). Antigen-binding fragments may also retain the ability to internalize into an antigen-expressing cell. In some embodiments, antigen-binding fragments also retain immune effector activity. It has been shown that fragments of a full-length antibody can perform the antigen-binding function of a full-length antibody. Examples of binding fragments encompassed within the term “antigen-binding fragment,” “antigen-binding domain,” or “antigen-binding portion” of an antibody include (i) a Fab fragment, a monovalent fragment consisting of the VL, VH, CL, and CH1 domains; (ii) a F(ab')₂ fragment, a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region; (iii) a Fd fragment consisting of the VH and CH1 domains; (iv) a Fv fragment consisting of the VL and VH domains of a single arm of an antibody; (v) a dAb fragment, which comprises a single variable domain, e.g., a VH domain (see, e.g., Ward et al. (1989) *Nature* 341:544-6; and Intl. Pub. No. WO 1990/005144); and (vi) an isolated complementarity determining region (CDR). Furthermore, although the two domains of the Fv fragment, VL and VH, are coded for by separate genes, they can be joined, using recombinant methods, by a synthetic linker that enables them to be made as a single protein chain in which the VL and VH regions pair to form monovalent molecules (known as single chain Fv (scFv)). See, e.g., Bird et al. (1988) *Science* 242:423-6; and Huston et al. (1988) *Proc. Natl. Acad. Sci. USA* 85:5879-83. Such single chain antibodies are also intended to be encompassed within the term “antigen-binding fragment” or “antigen-binding portion” of an antibody, and are known in the art as an exemplary type of binding fragment that can internalize into cells upon binding (see, e.g., Zhu et al. (2010) 9:2131-41; He et al. (2010) *J. Nucl. Med.* 51:427-32; and Fitting et al. (2015) *MAbs* 7:390-402). In certain embodiments, scFv molecules may be incorporated into a fusion protein. Other forms of single chain antibodies, such as diabodies, are also encompassed. Diabodies are bivalent, bispecific antibodies in which VH and VL domains are expressed on a single polypeptide chain, but using a linker that is too short to allow for pairing between the two domains on the same chain, thereby forcing the domains to pair with complementary domains of another chain and creating two antigen-binding sites (see e.g., Holliger et al. (1993) *Proc. Natl. Acad. Sci. USA* 90:6444-8; and Poljak et al. (1994) *Structure* 2:1121-3). Antigen-binding fragments are obtained using conventional techniques

known to those of skill in the art, and the binding fragments are screened for utility (e.g., binding affinity, internalization) in the same manner as are intact antibodies. Antigen-binding fragments may be prepared by cleavage of the intact protein, e.g., by protease or chemical cleavage.

[0093] “Internalizing” as used herein in reference to an antibody or antigen-binding fragment refers to an antibody or antigen-binding fragment that is capable of being taken through the cell’s lipid bilayer membrane to an internal compartment (i.e., “internalized”) upon binding to the cell, typically into a degradative compartment in the cell. For example, an internalizing anti-eribulin antibody is one that is capable of being taken into the cell after binding to eribulin on the cell membrane. In some embodiments, the antibody or antigen-binding fragment used in the ADCs disclosed herein targets a cell surface antigen (e.g., eribulin) via an internalizing antibody or internalizing antigen-binding fragment (allowing the ADC to transfer through the cellular membrane after antigen-binding).

[0094] The term “mesothelin” or “MSLN,” as used herein, refers to any native form of human mesothelin (MSLN). The term encompasses full-length mesothelin (e.g., NCBI Reference Sequence: AAC50348.1; SEQ ID NO: 271), as well as any form of human mesothelin that results from cellular processing. The term also encompasses naturally occurring variants of mesothelin, including but not limited to splice variants, allelic variants, and isoforms. Mesothelin can be isolated from a human, or may be produced recombinantly or by synthetic methods. The term may also encompass any synthetic variant to which an anti-mesothelin antibody, e.g., an antibody disclosed herein, and/or antigen-binding fragment, can specifically bind.

[0095] The term “anti-MSLN antibody” or “antibody that specifically binds MSLN” refers to any form of antibody or fragment thereof that specifically binds MSLN, and encompasses monoclonal antibodies (including full length monoclonal antibodies), polyclonal antibodies, and biologically functional antibody fragments so long as they specifically bind MSLN. Preferably the anti-MSLN antibody used in the ADCs disclosed herein is an internalizing antibody or internalizing antibody fragment. 345A12-HC15-LC4 (“345A12”) is an exemplary internalizing anti-human MSLN antibody. An anti-MSLN antibody may be conjugated to a drug, e.g., eribulin, via a linker. Exemplary antibody-drug conjugates comprising anti-MSLN antibodies are known in the literature and include MORAb-109. The structure of MORAb-109 is as shown in US Patent Serial No. 11,572,414, which is

incorporated herein by reference for all ADC and linker-payload structures and methods of synthesizing those structures. In some embodiments, MORAb-109 comprises an anti-MSLN antibody or antigen-binding fragment, 345A12-HC15-LC4, a cleavable linker comprising Mal-(PEG)₂-Val-Cit-pAB, and a payload comprising eribulin (see Table 1).

[0096] The term “folate receptor alpha” or “FRA,” as used herein, refers to any native form of human FRA. The term encompasses full-length FRA (e.g., NCBI Reference Sequence: NP_000793; SEQ ID NO: 270), as well as any form of human FRA that results from cellular processing. The term also encompasses naturally occurring variants of FRA, including but not limited to splice variants, allelic variants, and isoforms. FRA can be isolated from a human or may be produced recombinantly or by synthetic methods.

[0097] The term “anti-FRA antibody” or “antibody that specifically binds FRA” refers to any form of antibody or fragment thereof that specifically binds FRA, and encompasses monoclonal antibodies (including full length monoclonal antibodies), polyclonal antibodies, and biologically functional antibody fragments so long as they specifically bind FRA. Preferably the anti-FRA antibody used in the ADCs disclosed herein is an internalizing antibody or internalizing antibody fragment. MORAb-003 is an exemplary internalizing anti-human FRA antibody. As used herein, the term “MORAb-003” and “farletuzumab” are interchangeable. An anti-FRA antibody may be conjugated to a drug, e.g., eribulin, via a linker. Exemplary antibody-drug conjugates comprising anti-FRA antibodies are known in the literature and include MORAb-202. The structure of MORAb-202 is as shown in US Patent Serial No. 10,322,192, which is incorporated herein by reference for all ADC and linker-payload structures and methods of synthesizing those structures. In some embodiments, MORAb-202 comprises the anti-FRA antibody farletuzumab, a cleavable linker comprising Mal-(PEG)₂-Val-Cit-pAB, and a payload comprising eribulin (see Table 1).

Table 1. MORAb-202 and MORAb-109

	Target	Antibody	Linker	Payload
MORAb-202	FRA	MORAb-003 (farletuzumab)	Mal-(PEG) ₂ -Val-Cit-pAB	Eribulin
MORAb-109	MSLN	345A12	Mal-(PEG) ₂ -Val-Cit-pAB	Eribulin

[0098] The term “human epidermal growth factor receptor 2,” “HER2,” or “HER2/neu,” as used herein, refers to any native form of human HER2. The term encompasses full-length

her2 (e.g., NCBI Reference Sequence: NP_004439.2; SEQ ID NO: 272), as well as any form of human her2 that results from cellular processing. The term also encompasses naturally occurring variants of her2, including but not limited to splice variants, allelic variants, and isoforms. Her2 can be isolated from human, or may be produced recombinantly or by synthetic methods. An anti-HER2 antibody may be conjugated to a drug, e.g., eribulin, via a linker. Exemplary ADCs comprising anti-HER2 antibodies are known in the literature.

[0099] The term “anti-ID antibody” or “anti-idiotypic antibody” refers to an antibody that binds the idiotype, i.e., variable region, of a second antibody. Exemplary anti-ID antibodies include anti-farletuzumab antibodies (e.g., 2G9) and anti-345A12 antibodies (e.g., M000053) as described herein.

[00100] The term “anti-eribulin antibody” or “antibody that specifically binds eribulin” or “eribulin-specific antibody” refers to any form of antibody or fragment thereof that specifically binds eribulin, and encompasses monoclonal antibodies (including full-length monoclonal antibodies), polyclonal antibodies, and biologically functional antibody fragments so long as they specifically bind eribulin. In some embodiments, 5E4 is an exemplary eribulin-specific antibody.

[00101] The term “anti-linker antibody” refers to any form of antibody or antigen-binding fragment thereof that specifically binds a linker. As an example, an “anti-VCP antibody” or “antibody that specifically binds VCP” or “VCP-specific antibody” or “antibody that specifically binds a linker-payload comprising VCP” is an antibody that binds a linker comprising valine-citruline-p-aminobenzyloxycarbonyl (VCP), and encompasses monoclonal antibodies (including full-length monoclonal antibodies), polyclonal antibodies, and biologically functional antibody fragments so long as they specifically bind VCP. In some embodiments, 11G6 is an exemplary VCP-specific antibody. An anti-linker antibody may bind the linker when conjugated to an antibody and/or payload, or it may bind only when the linker is liberated from one or more of the other components, or it may bind in both contexts.

[00102] As used herein, the terms “specific,” “specifically binds,” and “binds specifically” refer to the selective binding of an antibody to a target antigen epitope. Antibodies can be tested for specificity of binding by comparing binding to an appropriate antigen with binding to an irrelevant antigen or antigen mixture under a given set of conditions. Methods for measuring antibody binding affinity and kinetics are known in the art and include, e.g.,

Biacore. If the antibody binds to the appropriate antigen with at least 2, 5, 7, or 10 times greater affinity than to the irrelevant antigen or antigen mixture, then it is considered to be specific. A “specific antibody” or “target-specific antibody” is one that only binds the target antigen (e.g., farletuzumab, 345A12, or human IgG Fc), but does not bind (or exhibits minimal binding to) other antigens.

[00103] The term “epitope” refers to the portion of an antigen capable of being recognized and specifically bound by an antibody. When the antigen is a polypeptide, epitopes can be formed from contiguous amino acids or noncontiguous amino acids juxtaposed by tertiary folding of the polypeptide. The epitope bound by an antibody may be identified using any epitope mapping technique known in the art, including X-ray crystallography for epitope identification by direct visualization of the antigen-antibody complex, as well as monitoring the binding of the antibody to fragments or mutated variations of the antigen, or monitoring solvent accessibility of different parts of the antibody and the antigen. Exemplary strategies used to map antibody epitopes include, but are not limited to, array-based oligo-peptide scanning, limited proteolysis, site-directed mutagenesis, high-throughput mutagenesis mapping, hydrogen-deuterium exchange, and mass spectrometry (see, e.g., Gershoni et al. (2007) 21:145-56; and Hager-Braun and Tomer (2005) Expert Rev. Proteomics 2:745-56).

[00104] Competitive binding and epitope binning can also be used to determine antibodies sharing identical or overlapping epitopes. Competitive binding can be evaluated using a cross-blocking assay, such as the assay described in “Antibodies, A Laboratory Manual,” Cold Spring Harbor Laboratory, Harlow and Lane (1st edition 1988, 2nd edition 2014). In some embodiments, competitive binding is identified when a test antibody or binding protein reduces binding of a reference antibody or binding protein to a target antigen such as farletuzumab or 345A12 (e.g., a binding protein comprising CDRs and/or variable domains selected from those identified in Tables 1-3 and Tables 6-8), by at least about 50% in the cross-blocking assay (e.g., 50%, 60%, 70%, 80%, 90%, 95%, 99%, 99.5%, or more, or any percentage in between), and/or vice versa. In some embodiments, competitive binding can be due to shared or similar (e.g., partially overlapping) epitopes, or due to steric hindrance where antibodies or binding proteins bind at nearby epitopes (see, e.g., Tzartos, Methods in Molecular Biology (Morris, ed. (1998) vol. 66, pp. 55-66)). In some embodiments, competitive binding can be used to sort groups of binding proteins that share similar epitopes. For example, binding proteins that compete for binding can be “binned” as a group of binding

proteins that have overlapping or nearby epitopes, while those that do not compete are placed in a separate group of binding proteins that do not have overlapping or nearby epitopes.

[00105] The term " k_{on} " or " k_a " refers to the on-rate constant for association of an antibody to the antigen to form the antibody/antigen complex. The rate can be determined using standard assays, such as a surface plasmon resonance, biolayer interferometry, or ELISA assay.

[00106] The term " k_{off} " or " k_d " refers to the off-rate constant for dissociation of an antibody from the antibody/antigen complex. The rate can be determined using standard assays, such as a surface plasmon resonance, biolayer interferometry, or ELISA assay.

[00107] The term " K_D " refers to the equilibrium dissociation constant of a particular antibody-antigen interaction. K_D is calculated by k_a/k_d . The rate can be determined using standard assays, such as a surface plasmon resonance, biolayer interferometry, or ELISA assay.

[00108] The term " p " or "drug loading" or "drug:antibody ratio" or "drug-to-antibody ratio" or "DAR" refers to the number of drug moieties per antibody moiety, i.e., drug loading, or the number of -L-D moieties per antibody or antigen-binding fragment (Ab) in ADCs of Formula (I). In ADCs comprising an eribulin drug moiety, " p " refers to the number of eribulin moieties linked to the antibody moiety. For example, if two eribulin moieties are linked to an antibody moiety, $p = 2$. In compositions comprising multiple copies of ADCs of Formula (I), "average p " refers to the average number of -L-D moieties per antibody or antigen-binding fragment in a population of ADCs, also referred to as "average drug loading."

[00109] A "linker" or "linker moiety" is used herein to refer to any chemical moiety that is capable of covalently joining a compound, usually a drug moiety such as eribulin, to another moiety such as an antibody moiety. Linkers can be susceptible to or substantially resistant to acid-induced cleavage, peptidase-induced cleavage, light-based cleavage, esterase-induced cleavage, and/or disulfide bond cleavage, at conditions under which the compound or the antibody remains active.

[00110] The term "payload" is used herein to refer to a chemical compound or a biological macromolecule that is capable of being conjugated to an antibody. A payload may be capable of modulating a biological process and/or have biological activity. The terms "agent," "therapeutic agent," "drug," or "drug moiety" are interchangeable with "payload" herein. In some embodiments, the payload is eribulin.

[00111] The term “linker-payload” is used herein to refer to a conjugate comprising a linker (e.g., VCP) and a payload (e.g., eribulin). Unless otherwise indicated, reference to a “linker-payload” as used herein refers to a linker-payload metabolite that is not conjugated to an antibody or ADC. In some embodiments, an antibody disclosed herein is capable of binding to an epitope present in a linker-payload.

[00112] The term “eribulin” or “eribulin monomer,” as used herein, refers to a synthetic analog of halichondrin B, a macrocyclic compound that was originally isolated from the marine sponge *Halichondria okadae*. Eribulin is a microtubule dynamics inhibitor, which is thought to bind tubulin and induce cell cycle arrest at the G2/M phase by inhibiting mitotic spindle assembly. The term “eribulin mesylate” refers to the mesylate salt of eribulin, which is marketed under the trade name Halaven™. Exemplary eribulin analogs include those shown and described in U.S. Patent No. 6,214,865 and U.S. Patent No. 6,653,341, which are incorporated herein by reference for the disclosed eribulin structures and methods of synthesizing those structures. The structure of eribulin is shown below.

[00113] The term “homolog” refers to a molecule which exhibits homology to another molecule, by for example, having sequences of chemical residues that are the same or similar at corresponding positions.

[00114] The term “inhibit” or “inhibition of,” as used herein, means to reduce by a measurable amount, and can include but does not require complete prevention or inhibition.

[00115] The term “cancer” refers to the physiological condition in mammals in which a population of cells is characterized by unregulated cell growth. Examples of cancers include, but are not limited to, carcinoma, lymphoma, blastoma, sarcoma, and leukemia. More particular examples of such cancers include squamous cell cancer, small cell lung cancer, nonsmall cell lung cancer, adenocarcinoma of the lung, squamous carcinoma of the lung, cancer of the peritoneum, hepatocellular cancer, gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, breast cancer (e.g., triple negative breast cancer), osteosarcoma, melanoma, colon cancer, colorectal cancer, endometrial (e.g., serous) or uterine cancer, salivary gland carcinoma, kidney cancer, liver cancer, prostate cancer, vulval cancer, thyroid cancer, hepatic carcinoma, and various types of head and neck cancers. Triple negative breast cancer refers to breast cancer that is negative for expression of the genes for estrogen receptor (ER), progesterone receptor (PR), or Her2/neu.

[00116] The terms “tumor” and “neoplasm” refer to any mass of tissue that results from excessive cell growth or proliferation, either benign or malignant, including precancerous lesions.

[00117] The term “tumor cell” refers to individual cells or the total population of cells derived from a tumor, including both non-tumorigenic cells and cancer stem cells. As used herein, the term “tumor cell” will be modified by the term “non-tumorigenic” when referring solely to those tumor cells lacking the capacity to renew and differentiate to distinguish those tumor cells from cancer stem cells.

[00118] The terms “subject” and “patient” are used interchangeably herein to refer to any animal, such as any mammal, including but not limited to, humans, non-human primates, rodents, and the like. In some embodiments, the mammal is a mouse. In some embodiments, the mammal is a human.

[00119] As used herein, “to treat” or “therapeutic” and grammatically related terms refer to any improvement of any consequence of disease, such as prolonged survival, less morbidity, and/or a lessening of side effects which are the byproducts of an alternative therapeutic modality. As is readily appreciated in the art, full eradication of disease is encompassed but not required for a treatment act. “Treatment” or “treat,” as used herein, refers to the administration of a described antibody, antigen-binding fragment, and/or ADC to a subject, e.g., a patient. The treatment can be to cure, heal, alleviate, relieve, alter, remedy, ameliorate, palliate, improve or affect the disorder, the symptoms of the disorder or the predisposition toward the disorder, e.g., a cancer. In some embodiments, in addition to treating a subject with a condition, a composition disclosed herein can also be provided prophylactically to prevent or reduce the likelihood of developing that condition.

[00120] In some embodiments, a labeled antibody, antigen-binding fragment, and/or ADC is used. A label is any moiety attached to an antibody that facilitates its detection in an assay in which the antibody is used. In some embodiments, the label is a detectable label. Suitable “labels” or “detectable labels” include fluorescent tags, radionuclides, enzymes, substrates, cofactors, inhibitors, fluorescent moieties, luminescent moieties, chemiluminescent moieties, electrochemiluminescent moieties, biotin, beads, magnetic particles, and the like. The terms “conjugated to a biotin” and “biotinylated” are used interchangeably herein.

[00121] For amino acid sequences, sequence identity and/or similarity may be determined using standard techniques known in the art, including, but not limited to, the local sequence

identity algorithm of Smith and Waterman (1981) Adv. Appl. Math. 2:482, the sequence identity alignment algorithm of Needleman and Wunsch (1970) J. Mol. Biol. 48:443, the search for similarity method of Pearson and Lipman (1988) Proc. Nat. Acad. Sci. USA 85:2444, computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group, 575 Science Drive, Madison, Wis.), the Best Fit sequence program described by Devereux et al. (1984) Nucl. Acid Res. 12:387-95, e.g., using the default settings, or by inspection. In some embodiments, percent identity is calculated by FastDB based upon the following parameters: mismatch penalty of 1; gap penalty of 1; gap size penalty of 0.33; and joining penalty of 30 ("Current Methods in Sequence Comparison and Analysis," Macromolecule Sequencing and Synthesis, Selected Methods and Applications, pp. 127-149 (1988), Alan R. Liss, Inc).

[00122] Generally, the amino acid homology, similarity, or identity between proteins disclosed herein and variants thereof, including variants of target antigens (such as farletuzumab or 345A12), variants of tubulin sequences, and variants of antibody variable domains (including individual variant CDRs), are at least 80% to the sequences depicted herein, e.g., homologies or identities of at least 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, almost 100%, or 100%.

[00123] In a similar manner, "percent (%) nucleic acid sequence identity" with respect to the nucleic acid sequence of the antibodies and other proteins identified herein is defined as the percentage of nucleotide residues in a candidate sequence that are identical with the nucleotide residues in the coding sequence of the antigen-binding protein. A specific method utilizes the BLASTN module of WU-BLAST-2 set to the default parameters, with overlap span and overlap fraction set to 1 and 0.125, respectively.

[00124] While the site or region for introducing an amino acid sequence variation is predetermined, the mutation per se need not be predetermined. For example, in order to optimize the performance of a mutation at a given site, random mutagenesis may be conducted at the target codon or region and the expressed antigen-binding protein CDR variants screened for the optimal combination of desired activity. Techniques for making substitution mutations at predetermined sites in DNA having a known sequence are well known, for example, MI3 primer mutagenesis and PCR mutagenesis.

[00125] The term "immunodepletion" or "antibody depletion" refers to an assay whereby a target antigen, e.g., an ADC, antibody, antigen-binding fragment, or linker-payload

conjugate, is depleted or removed from a solution using an antibody that specifically binds to said antigen.

[00126] The terms “metabolite” and “ADC metabolite” refer to components of an ADC that, through chemical, biochemical, or enzymatic processes are released from the ADC. ADC metabolites may include ADCs with DAR lower than starting DAR, antibodies, antigen-binding fragments, linker-payload conjugates, free payload moieties, free linker conjugates (i.e., without a payload attached), or any combination thereof.

Antibodies and Antigen-Binding Fragments

[00127] The present disclosure provides antibodies or antigen-binding fragments thereof for use in methods of detecting and quantifying intact antibody-drug conjugates or constituent antibody-drug conjugate parts such as a linker-payload, e.g., Mal-(PEG)₂-VCP-eribulin or albumin-Mal-(PEG)₂-VCP-eribulin, in a biological sample.

[00128] In some embodiments, the antibody or antigen-binding fragments may bind to a target antigen with a dissociation constant (K_D) of ≤ 1 mM, ≤ 100 nM or ≤ 10 nM, or any amount in between, as measured by, e.g., BIAcore® analysis. In certain embodiments, the K_D is 1 pM to 500 pM. In some embodiments, the K_D is between 500 pM to 1 μ M, 1 μ M to 100 nM, or 100 nM to 10 nM.

[00129] In some embodiments, the antibody moiety is a four-chain antibody (also referred to as an immunoglobulin), comprising two heavy chains and two light chains. In some embodiments, the antibody moiety is a two-chain half body (one light chain and one heavy chain), or an antigen-binding fragment of an immunoglobulin.

[00130] In some embodiments, the antibody moiety is an antigen-binding fragment thereof.

Anti-Farletuzumab Antibodies and Antigen-Binding Fragments

[00131] The present disclosure provides antibody and antigen-binding fragments thereof that specifically bind to an antibody-drug conjugate comprising farletuzumab and/or to farletuzumab or an antigen-binding fragment thereof. All references herein to “anti-farletuzumab” antibodies encompass antibodies that bind to farletuzumab, to an antibody-drug conjugate comprising farletuzumab, or to an antigen-binding fragment thereof.

[00132] In some embodiments, an anti-farletuzumab antibody or antigen-binding fragment, e.g., one used in any of the assays disclosed herein, may comprise a paired set of heavy and

light chain variable domains taken from those listed in Table 3, or the set of six CDR sequences from the paired heavy and light chain set, e.g., a set of CDRs listed in Tables 1-2. In some embodiments, an antibody or antigen-binding fragment further comprises human heavy and light chain frameworks (optionally with one or more backmutations to improve binding affinity) and/or human heavy and light chain constant domains or fragments thereof. For instance, the antibody or antigen-binding fragment may comprise a human IgG heavy chain constant domain (such as an IgG1) and a human kappa or lambda light chain constant domain. In some embodiments, the antibody or antigen-binding fragment comprises a human immunoglobulin G subtype 1 (IgG1) heavy chain constant domain (SEQ ID NO: 81) with a human Ig kappa light chain constant domain (SEQ ID NO: 82).

[00133] Amino acid and nucleic acid sequences of exemplary anti-farletuzumab antibodies of the present disclosure are set forth in Tables 2-6.

Table 2. Amino acid sequences of Kabat CDRs for an anti-farletuzumab antibody

mAb	IgG chain	SEQ ID	Amino acid sequence
2G9	HC CDR1	1	TYAVH
	HC CDR2	2	VIWGGKTDYNAIFIS
	HC CDR3	3	SGVLPYPLDY
	LC CDR1	4	RTSENIYRYLA
	LC CDR2	5	FAKTLAE
	LC CDR3	6	QQHYGIPLT

Table 3. Amino acid sequences of IMGT CDRs for an anti-farletuzumab antibody

mAb	IgG chain	SEQ ID	Amino acid sequence
2G9	HC CDR1	7	GFSLSTYA
	HC CDR2	8	IWSGGKT
	HC CDR3	9	ARSGVLPYPLDY
	LC CDR1	10	ENIYRY
	LC CDR2	11	FAK
	LC CDR3	12	QQHYGIPLT

Table 4. Amino acid sequences of variable regions for an anti-farletuzumab antibody

mAb	IgG chain	SEQ ID	Amino acid sequence
2G9	VH	13	QVQLKQSGPGLVQPSSLSITCTVSGFSLSTYAVHWV RQSPGEGLEWLGVIWSGGKTDYNAIFISRLSISKDNS KSQVFFTMNSLQPIDTGIYYCARSGVLPYPLDYWGQG TSVTVSS
	VL	14	DIQMTQSPVLSAPVGETVTITCRTSENIYRYLAWYQ QKQGKSPQLLVHFAKTLAEGVPSRFSGSGSGTQFSLK INNLPEDFGRIYCCQHYGIPLTFGVGTNLELK

Table 5. Amino acid sequences of full-length antibody chains for an anti-farletuzumab antibody

mAb	IgG chain	SEQ ID	Amino acid sequence
2G9	Heavy chain	15	QVQLKQSGPGLVQPSSLSITCTVSGFSLSTYAVHWV RQSPGEGLEWLGVIWSGGKTDYNAIFISRLSISKDNS KSQVFFTMNSLQPIDTGIYYCARSGVLPYPLDYWGQG TSVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVK DYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSS VVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD KTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQ YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL YSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL SPGK
	Light chain	16	DIQMTQSPVLSAPVGETVTITCRTSENIYRYLAWYQ QKQGKSPQLLVHFAKTLAEGVPSRFSGSGSGTQFSLK INNLPEDFGRIYCCQHYGIPLTFGVGTNLELK RTVAAPSVFIFPPSDEQLKSGTASVVCCLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTTL SKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Table 6. Nucleic acid sequences of full-length antibody chains for an anti-farletuzumab antibody

mAb	IgG chain	SEQ ID	Nucleic acid sequence
2G9	Heavy chain	83	CAGGTGCAGCTGAAGCAGTCAGGACCTGGCCTAGTCAGCCCTC ACAGAGCCTGTCCATCACCTGCACAGTCTCTGGTTTCTCATTA GTACCTATGCTGTTCACTGGGTTGCCAGTCTCCAGGAGAGGGT CTGGAGTGGCTGGGAGTGATATGGAGTGGTGGAAAGACAGACTA TAATGCAATTTTCATATCCAGACTGAGTATCAGCAAGGACAATT CCAAGAGTCAAGTTTCTTTACAATGAACAGTCTTCAGCCTATT GACACAGGCATATATTACTGTGCCAGATCCGGGGTCTCCCCCTA TCCTTTGGACTACTGGGGTCAAGGTACCTCAGTCACCGTCTCCT CAGCCTCCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCTCC TCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGT CAAGGACTACTTCCCCGAACCGGTGACGGTGTCTGTGAACCTCAG GCGCCCTGACCAGCGCGTGCACACCTTCCCGGCTGTCTACAG TCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACA AGCCCAGCAACACCAAGGTGGACAAGAAAGTTGAGCCCAAATCT TGTGACAAAATCACACATGCCACCGTGCCAGCACCTGAACT CCTGGGGGACCGTCAGTCTTCTCTTCCCCCAAACCCAAAGG ACACCCTCATGATCTCCCGGACCCCTGAGGTACATGCGTGGTG GTGGACGTGAGCCACGAAGACCTGAGGTCAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGG AGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCTTCACC GTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAA GGTCTCCAACAAAGCCCTCCAGCCCCCATCGAGAAAACCATCT CCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCTG CCCCCATCCCGGATGAGCTGACCAAGAACCAGGTGAGCCTGAC CTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCGTGGAGT GGGAGAGCAATGGGCAGCCGGAGAACAACCTACAAGACCACGCCT CCCGTGCTGGACTCCGACGGCTCCTTCTTCTTATATTCAAAGCT CACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCAT GCTCCGTGATGCATGAGGCTCTGCACAACCCTACACGCAGAAG AGCCTCTCCCTGTCTCCCGGAAA

mAb	IgG chain	SEQ ID	Nucleic acid sequence
	Light chain	84	GACATCCAGATGACTCAGTCTCCAGTCTCCCTATCTGCACCTGT GGGAGAACTGTCAACCATCACATGTGCAACAAGTGAGAATATTT ACAGGTATTTAGCATGGTATCAGCAGAAACAGGGAAAATCTCCT CAGCTCCTGGTCCATTTTGCAAAAACCTTGGCAGAAGGTGTGCC ATCAAGGTTCAGTGGCAGTGGATCAGGCACACAGTTTCTCTGA AGATCAACAACCTGCAGCCTGAAGATTTTGGGAGGTATTACTGT CAACAGCATTATGGTATTCTCTCACGTTCCGGTGTGGGACCAA CCTGGAGTTGAAACGAACGTGTGGCTGCACCATCTGTCTTCATCT TCCCGCCATCTGATGAGCAGTTGAAATCTGGAAGTGCCTCTGTT GTGTGCCTGCTGAATAACTTCTATCCAGAGAGGCCAAAGTACA GTGGAAGGTGGATAACGCCCTCCAATCGGGTAACCTCCAGGAGA GTGTCACAGAGCAGGACAGCAAGGACAGCACCTACAGCCTCAGC AGCACCTGACGCTGAGCAAAGCAGACTACGAGAAACACAAAGT CTACGCCCTGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCA CAAAGAGCTTCAACAGGGGAGAGTGT

[00134] In some embodiments, an anti-farletuzumab antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 1 (HCDR1), SEQ ID NO: 2 (HCDR2), and SEQ ID NO: 3 (HCDR3); and three LCDRs comprising SEQ ID NO: 4 (LCDR1), SEQ ID NO: 5 (LCDR2), and SEQ ID NO: 6 (LCDR3) as defined by the Kabat numbering system (Kabat, Sequences of Proteins of Immunological Interest (National Institutes of Health, Bethesda, Md. (1987 and 1991))).

[00135] In some embodiments, an anti-farletuzumab antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 7 (HCDR1), SEQ ID NO: 8 (HCDR2), and SEQ ID NO: 9 (HCDR3); and three LCDRs comprising SEQ ID NO: 10 (LCDR1), SEQ ID NO: 11 (LCDR2), and SEQ ID NO: 12 (LCDR3), as defined by the IMGT numbering system (International ImMunoGeneTics Information System (IMGT®)).

[00136] In some embodiments, an anti-farletuzumab antibody or antigen-binding fragment provided herein comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 13. In some embodiments, an anti-farletuzumab antibody or antigen-binding fragment thereof provided herein comprises a light chain variable region comprising an amino acid sequence of SEQ ID NO: 14.

[00137] In some embodiments, an anti-farletuzumab antibody or antigen-binding fragment thereof provided herein comprises three HCDRs from the heavy chain variable region comprising SEQ ID NO: 13. In some embodiments, the anti-farletuzumab antibody or antigen-binding fragment comprises three LCDRs from the light chain variable region comprising SEQ ID NO: 14.

[00138] In some embodiments, an anti-farletuzumab antibody or antigen-binding fragment thereof provided herein comprises a heavy chain variable region with at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 13. In some embodiments, an anti-farletuzumab antibody or antigen-binding fragment thereof provided herein comprises a light chain variable region with at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 14.

[00139] In some embodiments, an antigen-binding fragment disclosed herein is a variant that retains farletuzumab binding specificity. In some embodiments, the antigen-binding fragment retains farletuzumab binding by comprising three HCDRs comprising amino acid sequences of SEQ ID NO: 1 (HCDR1), SEQ ID NO: 2 (HCDR2), and SEQ ID NO: 3 (HCDR3); and three LCDRs comprising SEQ ID NO: 4 (LCDR1), SEQ ID NO: 5 (LCDR2), and SEQ ID NO: 6 (LCDR3) as defined by the Kabat numbering system. In some embodiments, the antigen-binding fragment comprises three heavy chain CDRs (HCDR1, HCDR2, and HCDR3) comprising three HCDRs comprising amino acid sequences of SEQ ID NO: 7 (HCDR1), SEQ ID NO: 8 (HCDR2), and SEQ ID NO: 9 (HCDR3); and three LCDRs comprising SEQ ID NO: 10 (LCDR1), SEQ ID NO: 11 (LCDR2), and SEQ ID NO: 12 (LCDR3), as defined by the IMGT numbering system. In some embodiments, the antigen-binding fragments disclosed herein may retain farletuzumab binding by comprising a VH domain comprising an amino acid sequence comprising SEQ ID NO: 13 and a VL domain comprising an amino acid sequence comprising SEQ ID NO: 14.

[00140] In various embodiments, an anti-farletuzumab antibody disclosed herein comprises a human IgG heavy chain constant domain. In some embodiments, the IgG heavy chain constant domain is IgG1.

[00141] In various embodiments, an anti-farletuzumab antibody disclosed herein comprise a human Ig kappa light chain constant region. In various embodiments, the anti-farletuzumab antibodies comprise a human Ig lambda light chain constant region.

[00142] In some embodiments, an anti-farletuzumab antibody or antigen-binding fragment provided herein comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 15. In some embodiments, an anti-farletuzumab antibody or antigen-binding fragment thereof provided herein comprises a light chain comprising an amino acid sequence of SEQ ID NO: 16.

[00143] In some embodiments, the anti-farletuzumab antibody or antigen-binding fragment is antibody 2G9.

[00144] In some embodiments, an anti-farletuzumab antibody or antigen-binding fragment provided herein is conjugated to a label. In some embodiments, the anti-farletuzumab antibody or antigen-binding fragment is conjugated to a fluorescent tag. In some embodiments, the anti-farletuzumab antibody or antigen-binding fragment is conjugated to a biotin moiety. In some embodiments, an anti-farletuzumab antibody provided herein is conjugated to streptavidin. In some embodiments, the anti-farletuzumab antibody or antigen-binding fragment is conjugated to an enzyme reporter. In some embodiments, the anti-farletuzumab antibody or antigen-binding fragment is conjugated to a bead. In some embodiments, the bead is an agarose bead or a magnetic bead.

[00145] In some embodiments, an anti-farletuzumab antibody or antigen-binding fragment provided herein is conjugated to an agarose bead or a magnetic bead.

[00146] In some embodiments, an anti-farletuzumab antibody or antigen-binding fragment provided herein is biotinylated.

[00147] In some embodiments, an anti-farletuzumab antibody or antigen-binding fragment provided herein specifically binds an ADC, antibody, or antigen-binding fragment comprising three heavy chain CDRs and three light chain CDRs as follows: HCDR1 comprising SEQ ID NO: 49, HCDR2 comprising SEQ ID NO: 50, HCDR3 comprising SEQ ID NO: 51; LCDR1 comprising SEQ ID NO: 52, LCDR2 comprising SEQ ID NO: 53, and LCDR3 comprising SEQ ID NO: 54, as defined by the Kabat numbering system. In some embodiments, an anti-farletuzumab antibody or antigen-binding fragment provided herein specifically binds an ADC, antibody, or antigen-binding fragment comprising three heavy chain CDRs and three light chain CDRs as follows: HCDR1 comprising SEQ ID NO: 55,

HCDR2 comprising SEQ ID NO: 56, HCDR3 comprising SEQ ID NO: 57; LCDR1 comprising SEQ ID NO: 58, LCDR2 comprising SEQ ID NO: 59, and LCDR3 comprising SEQ ID NO: 60, as defined by the IMGT numbering system.

[00148] In some embodiments, an anti-farletuzumab antibody or antigen-binding fragment provided herein specifically binds an ADC, antibody, or antigen-binding fragment comprising a heavy chain variable domain comprising a sequence of SEQ ID NO: 61 and a light chain variable domain comprising a sequence of SEQ ID NO: 62.

[00149] In some embodiments, an anti-farletuzumab antibody or antigen-binding fragment provided herein specifically binds an ADC, antibody, or antigen-binding fragment comprising a heavy chain of SEQ ID NO: 63 and a light chain sequence of SEQ ID NO: 64.

[00150] In some embodiments, an anti-farletuzumab antibody or antigen-binding fragment provided herein specifically binds farletuzumab or an ADC comprising farletuzumab.

[00151] In some embodiments, an anti-farletuzumab antibody or antigen-binding fragment provided herein specifically binds MORAb-202.

Anti-345A12 Antibodies and Antigen-Binding Fragments

[00152] The present disclosure also provides antibody and antigen-binding fragments thereof that specifically bind to an antibody-drug conjugate comprising 345A12 and/or to 345A12 or an antigen-binding fragment thereof. All references herein to “anti-345A12” antibodies encompass antibodies that bind to 345A12, to an antibody-drug conjugate comprising 345A12, or to an antigen-binding fragment thereof.

[00153] In some embodiments, an anti-345A12 antibody or antigen-binding fragment, e.g., one used in any of the assays disclosed herein, may comprise a paired set of heavy and light chain variable domains taken from those listed in Table 9, or the set of six CDR sequences from the paired heavy and light chain set, e.g., a set of CDRs listed in Tables 7-8. In some embodiments, an antibody or antigen-binding fragment further comprises human heavy and light chain frameworks (optionally with one or more backmutations to improve binding affinity) and/or human heavy and light chain constant domains or fragments thereof. For instance, the antibody or antigen-binding fragment may comprise a human IgG heavy chain constant domain (such as an IgG1) and a human kappa or lambda light chain constant domain. In some embodiments, the antibody or antigen-binding fragment comprises a human

immunoglobulin G subtype 1 (IgG1) heavy chain constant domain (SEQ ID NO: 81) with a human Ig lambda light chain constant domain (SEQ ID NO: 291).

[00154] Amino acid and nucleic acid sequences of exemplary anti-345A12 antibodies of the present disclosure are set forth in Tables 7-11.

Table 7. Amino acid sequences of Kabat CDRs for an anti-345A12 idiotypic antibody

mAb	IgG chain	SEQ ID	Amino acid sequence
Anti-345A12 idiotypic antibody (M000053)	HC CDR1	273	SYAMH
	HC CDR2	274	VISFDGSNKYYADSVKG
	HC CDR3	275	DESGSFSPYNWFDP
	LC CDR1	276	TGSRNIGAGYDVH
	LC CDR2	277	GNSNRPS
	LC CDR3	278	QSYDRSLSTWV

Table 8. Amino acid sequences of IMGT CDRs for an anti-345A12 idiotypic antibody

mAb	IgG chain	SEQ ID	Amino acid sequence
Anti-345A12 idiotypic antibody	HC CDR1	279	GFTFSSYA
	HC CDR2	280	ISFDGSNK
	HC CDR3	281	ARDESGSFSPYNWFDP
	LC CDR1	282	RSNIGAGYD
	LC CDR2	283	GNS
	LC CDR3	284	QSYDRSLSTWV

Table 9. Amino acid sequences of variable regions for an anti-345A12 idiotypic antibody

mAb	IgG chain	SEQ ID	Amino acid sequence
Anti-345A12 idiotypic antibody	VH	285	QVQLVQSGGGVVPGRSLRLSCAASGFTFSSYAMHWV RQAPGKGLEWVAVISFDGSNKYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCARDESGSFSPYNWFD PWGQGTLTIVSS
	VL	286	QSVLTQPPSVSGAPGQAVTISCTGSRNIGAGYDVHW YQQLPGTAPKLLIFGNSNRPSGVPGRFSGSKSGTSAS LAITGLRAEDEALYYCQSYDRSLSTWVFGGKVTVL

Table 10. Amino acid sequences of full-length antibody chains and scfv antibody fragments for an anti-345A12 idiotypic antibody

mAb	IgG chain	SEQ ID	Amino acid sequence
Anti-345A12 idiotypic antibody – scfv fragment	VH-VL	293	QVQLVQSGGGVVPGRSLRLSCAASGFTFSSYAMHWV RQAPGKGLEWVAVISFDGSNKYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCARDESGSFS PYNWFD PWGQGTLLTVSSSTRSSGGGGSGGGGSSAQS VLTQP PSVSGAPGQAVTISCTGSRNIGAGYDVHWYQQLPGT APKLLIFGNSNRPSGVPGFRFSGSKSGTSASLAITGLR AEDEALYYCQSYDRSLSTWVFGGGTKVTVLGAAADYK DDDDKGAA
Anti-345A12 idiotypic antibody	Heavy chain	287	QVQLVQSGGGVVPGRSLRLSCAASGFTFSSYAMHWV RQAPGKGLEWVAVISFDGSNKYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCARDESGSFS PYNWFD PWGQGTLLTVSSASTKGPSVFPLAPSSKSTSGGTAAL GCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL YSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVE PKSCDKHTCPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTK PREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKA LPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVS LTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSD GSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQ KSLSLSPEGK
	Light chain	288	QSVLTQPPSVSGAPGQAVTISCTGSRNIGAGYDVHW YQQLPGTAPKLLIFGNSNRPSGVPGFRFSGSKSGTSAS LAITGLRAEDEALYYCQSYDRSLSTWVFGGGTKVTVL GQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGA VTVAWKADSSPVKAGVETTTPSKQSNKYAASSYLSL TPEQWKSHKSYSCQVTHEGSTVEKTVAPTECS

Table 11. Nucleic acid sequences of heavy and light chain variable regions for an anti-345A12 idiotypic antibody

mAb	IgG chain	SEQ ID	Nucleic acid sequence
Anti-345A12 idiotypic antibody	VH	289	CAGGTGCAGCTGGTGCAGTCTGGGGGAGGCGTGGTCCAGCCTGGGA GGTCCCTGAGACTCTCCTGTGCAGCCTCTGGATTACCTTCAGTAG CTACGCTATGCACTGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAG TGGGTGGCAGTTATATCATTGATGGAAGTAATAAATACTACGCAG ACTCCGTGAAGGGCCGATTACCATCTCCAGAGACAATTCCAAGAA CACGCTGTATCTGCAAATGAACAGCCTGAGAGCTGAGGACACGGCT GTGTATTACTGTGCGAGAGATGAGAGTGGGAGCTTCAGTCCGTACA ACTGGTTCGACCCCTGGGGCCAGGGCACCTGGTCACCGTCTCCTC A
	VL	290	CAGTCTGTGTTGACGCAGCCGCCCTCAGTGTCTGGGGCCCCAGGAC AGGCGGTCAACATCTCCTGCACTGGGAGCCGTTCCAACATCGGGGC AGGCTATGATGTACACTGGTATCAGCAGCTTCCAGGAACAGCCCCC AAACTCCTCATCTTTGGAAACAGCAATCGGCCCTCAGGGGTTCTTG GCCGATTCTCTGGCTCCAAGTCTGGCACCTCAGCCTCCCTGGCCAT CACTGGACTCCGGGCTGAGGATGAGGCTCTTTATTACTGCCAGTCT TATGACAGAAGCCTGAGTACTTGGGTGTTCCGGCGGAGGGACCAAGG TCACCGTCCTA

[00155] In some embodiments, an anti-345A12 idiotypic antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 273 (HCDR1), SEQ ID NO: 274 (HCDR2), and SEQ ID NO: 275 (HCDR3); and three LCDRs comprising SEQ ID NO: 276 (LCDR1), SEQ ID NO: 277 (LCDR2), and SEQ ID NO: 278 (LCDR3) as defined by the Kabat numbering system.

[00156] In some embodiments, an anti-345A12 idiotypic antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 279 (HCDR1), SEQ ID NO: 280 (HCDR2), and SEQ ID NO: 281 (HCDR3); and three LCDRs comprising SEQ ID NO: 282 (LCDR1), SEQ ID NO: 283 (LCDR2), and SEQ ID NO: 284 (LCDR3), as defined by the IMGT.

[00157] In some embodiments, an anti-345A12 idiotypic antibody or antigen-binding fragment provided herein comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285. In some embodiments, an anti-345A12 idiotypic antibody or

antigen-binding fragment thereof provided herein comprises a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286.

[00158] In some embodiments, an anti-345A12 idiotypic antibody or antigen-binding fragment thereof provided herein comprises three HCDRs from the heavy chain variable region comprising SEQ ID NO: 285. In some embodiments, the anti-345A12 idiotypic antibody or antigen-binding fragment comprises three LCDRs from the light chain variable region comprising SEQ ID NO: 286.

[00159] In some embodiments, an anti-345A12 idiotypic antibody or antigen-binding fragment thereof provided herein comprises a heavy chain variable region with at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 285. In some embodiments, an anti-345A12 idiotypic antibody or antigen-binding fragment thereof provided herein comprises a light chain variable region with at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 286.

[00160] In some embodiments, an antigen-binding fragment disclosed herein is a variant that retains 345A12 binding specificity. In some embodiments, the antigen-binding fragment retains 345A12 binding by comprising three HCDRs comprising amino acid sequences of SEQ ID NO: 273 (HCDR1), SEQ ID NO: 274 (HCDR2), and SEQ ID NO: 275 (HCDR3); and three LCDRs comprising SEQ ID NO: 276 (LCDR1), SEQ ID NO: 277 (LCDR2), and SEQ ID NO: 278 (LCDR3) as defined by the Kabat numbering system. In some embodiments, the antigen-binding fragment comprises three heavy chain CDRs (HCDR1, HCDR2, and HCDR3) comprising three HCDRs comprising amino acid sequences of SEQ ID NO: 279 (HCDR1), SEQ ID NO: 280 (HCDR2), and SEQ ID NO: 281 (HCDR3); and three LCDRs comprising SEQ ID NO: 282 (LCDR1), SEQ ID NO: 283 (LCDR2), and SEQ ID NO: 284 (LCDR3), as defined by the IMGT numbering system. In some embodiments, the antigen-binding fragments disclosed herein may retain 345A12 binding by comprising a VH domain comprising an amino acid sequence comprising SEQ ID NO: 285 and a VL domain comprising an amino acid sequence comprising SEQ ID NO: 286.

[00161] In various embodiments, an anti-345A12 idiotypic antibody disclosed herein comprises a human IgG heavy chain constant domain. In some embodiments, the IgG heavy chain constant domain is IgG1.

[00162] In various embodiments, an anti-345A12 idiotypic antibody disclosed herein comprise a human Ig kappa light chain constant region. In various embodiments, the anti-345A12 idiotypic antibodies comprise a human Ig lambda light chain constant region.

[00163] In some embodiments, an anti-345A12 idiotypic antibody or antigen-binding fragment provided herein comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 287. In some embodiments, an anti-345A12 idiotypic antibody or antigen-binding fragment thereof provided herein comprises a light chain comprising an amino acid sequence of SEQ ID NO: 288.

[00164] In some embodiments, the anti-345A12 idiotypic antibody or antigen-binding fragment is antibody M000053.

[00165] In some embodiments, an anti-345A12 idiotypic antibody or antigen-binding fragment provided herein is conjugated to a label. In some embodiments, the anti-345A12 idiotypic antibody or antigen-binding fragment is conjugated to a fluorescent tag. In some embodiments, the anti-345A12 idiotypic antibody or antigen-binding fragment is conjugated to a biotin moiety. In some embodiments, the anti-345A12 idiotypic antibody is conjugated to streptavidin. In some embodiments, the anti-345A12 idiotypic antibody or antigen-binding fragment is conjugated to an enzyme reporter. In some embodiments, the anti-345A12 idiotypic antibody or antigen-binding fragment is conjugated to a bead. In some embodiments, the bead is an agarose bead or a magnetic bead.

[00166] In some embodiments, an anti-345A12 idiotypic antibody or antigen-binding fragment provided herein is conjugated to an agarose bead or a magnetic bead.

[00167] In some embodiments, an anti-345A12 idiotypic antibody or antigen-binding fragment provided herein is biotinylated.

[00168] In some embodiments, an anti-345A12 idiotypic antibody or antigen-binding fragment provided herein specifically binds an ADC, antibody, or antigen-binding fragment comprising three heavy chain CDRs and three light chain CDRs as follows: HCDR1 comprising SEQ ID NO: 65, HCDR2 comprising SEQ ID NO: 66, HCDR3 comprising SEQ ID NO: 67; LCDR1 comprising SEQ ID NO: 68, LCDR2 comprising SEQ ID NO: 69, and LCDR3 comprising SEQ ID NO: 70, as defined by the Kabat numbering system. In some

embodiments, an anti-345A12 idiotypic antibody or antigen-binding fragment provided herein specifically binds an ADC, antibody, or antigen-binding fragment comprising three heavy chain CDRs and three light chain CDRs as follows: HCDR1 comprising SEQ ID NO: 71, HCDR2 comprising SEQ ID NO: 72, HCDR3 comprising SEQ ID NO: 73; LCDR1 comprising SEQ ID NO: 74, LCDR2 comprising SEQ ID NO: 75, and LCDR3 comprising SEQ ID NO: 76, as defined by the IMGT numbering system.

[00169] In some embodiments, an anti-345A12 idiotypic antibody or antigen-binding fragment provided herein specifically binds an ADC, antibody, or antigen-binding fragment comprising a heavy chain variable domain comprising a sequence of SEQ ID NO: 77 and a light chain variable domain comprising a sequence of SEQ ID NO: 78.

[00170] In some embodiments, an anti-345A12 idiotypic antibody or antigen-binding fragment provided herein specifically binds an ADC, antibody, or antigen-binding fragment comprising a heavy chain of SEQ ID NO: 79 and a light chain sequence of SEQ ID NO: 80.

[00171] In some embodiments, an anti-345A12 idiotypic antibody or antigen-binding fragment provided herein specifically binds 345A12 or an ADC comprising 345A12.

[00172] In some embodiments, an anti-345A12 idiotypic antibody or antigen-binding fragment provided herein specifically binds MORAb-109.

Exemplary Antibodies Bound by Anti-ID Antibodies

[00173] Tables 12-15 set forth exemplary amino acid sequences of anti-FRA, anti-MSLN, and anti-HER2 antibodies. Amino acid sequences of human FRA, MSLN, and HER2 antibodies are disclosed in Table 16.

Table 12. Amino acid sequences of ADC mAb Kabat CDRs

mAb	IgG chain	SEQ ID NO	Amino acid sequence
Farletuzumab	HC CDR1	49	GYGLS
	HC CDR2	50	MISSGGSYTTYADSVKG
	HC CDR3	51	HGDDPAWFAY
	LC CDR1	52	SVSSSISSNNLH
	LC CDR2	53	GTSNLAS
	LC CDR3	54	QQWSSYPYMYT
	HC CDR1	65	SYAMS

mAb	IgG chain	SEQ ID NO	Amino acid sequence
345A12-HC15-LC4	HC CDR2	66	VIDISGNRFYADWVKG
	HC CDR3	67	VDSRAWGPFNL
	LC CDR1	68	QASQSIFSYLE
	LC CDR2	69	DASDLAS
	LC CDR3	70	QQGYTRSDVDNA
trastuzumab	HC CDR1	254	DTYIH
	HC CDR2	255	RIYPTNGYTRYADSVKG
	HC CDR3	256	WGGDGFYAMDY
	LC CDR1	257	RASQDVNTAVA
	LC CDR2	258	SASFLYS
	LC CDR3	259	QQHYTTPPT

Table 13. Amino acid sequences of ADC mAb IMGT CDRs

mAb	IgG chain	SEQ ID NO	Amino acid sequence
Farletuzumab	HC CDR1	55	GFTFSGYG
	HC CDR2	56	ISSGGSYT
	HC CDR3	57	ARHGDDPAWFAY
	LC CDR1	58	SSISSNN
	LC CDR2	59	GTS
	LC CDR3	60	QQWSSYPYMYT
345A12-HC15-LC4	HC CDR1	71	GIDLSSYA
	HC CDR2	72	IDISGNR
	HC CDR3	73	ARVDSRAWGPFNL
	LC CDR1	74	QSIFS
	LC CDR2	75	DAS
	LC CDR3	76	QQGYTRSDVDNA
trastuzumab	HC CDR1	260	GFNIKDTY
	HC CDR2	261	IYPTNGYT
	HC CDR3	262	SRWGGDGFYAMDY

mAb	IgG chain	SEQ ID NO	Amino acid sequence
	LC CDR1	263	QDVNTA
	LC CDR2	264	SAS
	LC CDR3	265	QQHYTTPPT

Table 14. Amino acid sequences of ADC mAb variable regions

mAb	IgG chain	SEQ ID NO	Amino acid sequence
Farletuzumab	VH	61	EVQLVESGGGVVQPGRSLRLSCSASGFT FSGYGLSWVRQAPGKGLEWVAMISGGGS YTYADSVKGRFAISRDNKNTLFLQMD SLRPEDTGVYFCARHGDDPAWFAYWGQG TPVTVSS
	VL	62	DIQLTQSPSSLSASVGDRVTITCSVSSS ISSNNLHWYQQKPGKAPKPIYGTSNLA SGVPSRFSGSGSGTDYTFITISLQPEDI ATYYCQQWSSYPMYTFGQGTKVEIK
345A12-HC15-LC4	VH	77	QVQLVESGGGVVQPGRSLRLSCAASGID LSSYAMSWVRQAPGKGLEWIGVIDISGN RFYADWVKGRFTISRDNKNTLYLQMSS LRAEDTAVYYCARVDSRAWGPFNLWGQG TLVTVSS
	VL	78	DYQMTQSPSSLSASVGDRVTITCQASQS IFSYLAWYQQKPGKAPKLLIYDASDLAS GVPSRFSGSGSGTDFTLTISLQCEDAA TYYCQQGYTRSDVDNAFGGGTKVEIK
trastuzumab	VH	266	EVQLVESGGGLVQPGGSLRLSCAASGFN IKDTYIHWVRQAPGKGLEWVARIYPTNG YTRYADSVKGRFTISADTSKNTAYLQMN SLRAEDTAVYYCSRWGGDGFYAMDYWGQ GTLVTVSS
	VL	267	DIQMTQSPSSLSASVGDRVTITCRASQD VNTAVAWYQQKPGKAPKLLIYSASFLYS GVPSRFSGSRSGTDFTLTISLQPEDFA TYYCQQHYTTPPTFGQGTKVEIK

Table 15. Amino acid sequences of full-length ADC mAb Ig chains

mAb	IgG chain	SEQ ID NO	Amino acid sequence
Farletuzumab	Heavy chain	63	EVQLVESGGGVVQPGRSLRLSCSASGFTFSGYG LSWVRQAPGKGLEWVAMISSGGSYTYADSVKG RFAISRDNKNTLFLQMDSLRPEDTGVYFCARH GDDPAWFAYWGQTPVTVSSASTKGPSVFPLAP SSKSTSGGTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQ TYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPC PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCV VVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQ YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL PAPIEKTISKAKGQPREPQVYTLPPSRDELTKN QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTT PPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSV MHEALHNHYTQKSLSLSPGK
	Light chain	64	DIQLTQSPSSLSASVGDRTVITCSVSSSISSNN LHWYQQKPKGKAPKRWIYGTSNLASGVPSRFSGS GSGTDYTFITISLQPEDIAITYCQQWSSYPMY TFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGT ASVVCLLNNFYPREAKVQWKVDNALQSGNSQES VTEQDSKSTYLSSTLTLSKADYEKHKVYACE VTHQGLSSPVTKSFNRGEC
345A12-HC15-LC4	Heavy chain	79	QVQLVESGGGVVQPGRSLRLSCAASGIDLSSYA MSWVRQAPGKGLEWIGVIDISGNRFYADWVKGR FTISRDNKNTLYLQMSLRAEDTAVYYCARVD SRAWGPFNLWGQGLTVTVSSASTKGPSVFPLAP SSKSTSGGTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQ TYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPC PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCV VVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQ YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL PAPIEKTISKAKGQPREPQVYTLPPSRDELTKN QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTT PPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSV MHEALHNHYTQKSLSLSPGK

mAb	IgG chain	SEQ ID NO	Amino acid sequence
	Light chain	80	DYQMTQSPSSLSASVGDRTITCQASQSI FSYL AWYQQKPGKAPKLLIYDASDLASGVPSRFSGSG SGTDFTLTITSSLCEDAATYYCQQGYTRSDVDN AFGGGKVEIKRTVAAPSVFIFPPSDEQLKSGT ASVVCLLNNFYPREAKVQWKVDNALQSGNSQES VTEQDSKDYSLSSSTLTLSKADYEKHKVYACE VTHQGLSSPVTKSFNRGEC
trastuzumab	Heavy chain	268	EVQLVESGGGLVQPGGSLRLSCAASGFNICKDY IHWVRQAPGKGLEWVARIYPTNGYTRYADSVKG RFTISADTSKNTAYLQMNSLRAEDTAVYYCSRW GGDGFYAMDYWGQGTLLTVSSASTKGPSVFPLA PSSKSTSGGTAALGCLVKDYFPEPVTISWNSGA LTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPPKSCDKTHTCP PCPAPPELLGGPSVFLFPPKPKDTLMISRTPEVT CVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE EQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNK ALPAPIEKTISKAKGQPREPQVYTLPPSRDELTA KNQVSLTCLVKGFPYSDIAVEWESNGQPENNYK TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS SVMHEALHNHYTQKSLSLSPGK
	Light chain	269	DIQMTQSPSSLSASVGDRTITCRASQDVNTAV AWYQQKPGKAPKLLIYSASFVSGVPSRFSGSR SGTDFTLTITSSLPEDFATYYCQQHYTTPPTFG QGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASV VCLLNNFYPREAKVQWKVDNALQSGNSQESVTE QDSKDYSLSSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC

Table 16. Amino acid sequences of antibodies and constant domains

mAb or constant domain	SEQ ID NO	Amino acid sequence
Human FRA	270	MAQRMTTQLLLLVWVAVVGEAQTRIAWARTELLNVCMAKHHKE KPGPEDKLHEQCRPWRKNACCSTNTSQEAHKDVSYLRFNWNHCG EMAPACKRHF IQDTCLYECSPNLGPWIIQQVDQSWRKERVNLNPLC KEDCEQWWEDCRTSYTCKSNWHKGWNWTS GFNKA VGAACQPFHF YFPTPTVLCNEI WTHSYKVSNSRSGRCIQMWFDPAQGNPNEEV ARFYAAAMSGAGPWAAPFLLSLALMLLWLLS

mAb or constant domain	SEQ ID NO	Amino acid sequence
Human MSLN	271	MALQRLDPCWSCGDRPGSLLFLLFSLGWVHPARTLAGETGTESAP LGGVLTTPHNISSLSRQLLGFPACAEVSGLSTERVRELAVALAQK NVKLSTEQLRCLAHRLSEPPEDLDALPLDLLLFLNPDAFSGPQAC TRFFSRITKANVDLLPRGAPERQRLPAALACWGVRSLLSEADV RALGGLACDLPGRFVAESAEVLLPRLVSCPGPLDQDQQAARAAL QGGGPPYGPPSTWSVSTMDALRGLLPVLGQPIIRSIPQGIVAAR QRSSRDPSWRQPRTLIRPRFRREVEKTACPSGKKAREIDESLIF YKKWELEACVDAALLATQMDRVNAIPFTYEQLDVLKHKLDELYPQ GYPESVIQHLGYLFLKMSPEDIRKWNVTSLKALLEVDKGHEM SPQAPRRPLPQVATLIDRFVKGRLDKDTLDTLTAFFPGYLCSL SPEELSSVPPSSIWAVRPQDLDTCDPRQLDVLYPKARLAFQNMNG SEYFVKIQSFLGGAPTEDLKALSQQNVSMDLATFMKLRTDAVLP TVAEVQKLLGPHVEGLKAEERHRPVRDWILRQRQDDDLTLGLGLQ GGIPNGYLVLDLSVQETLSGTPCLLGPGPVLTVLALLLASTLA
Human HER2	272	MELAALCRWGLLLALLPPGAASTQVCTGTMKRLRPASPETHLDM LRHLYQGCQVVGQNLLETYLPTNASLSFLQDIQEVQGYVLIHNNQ VRQVPLQRLRIVRGTLFEDNYALAVLDNGDPLNNTTPTVGASPG GLRELQLRSLTEILKGGVLIQRNPQLCYQDTILWKDIFHKNNQLA LTLIDTNRSRACHPCSPMCKGSRGWGESSEDCQSLTRTVCAAGCA RCKGPLPTDCCHEQCAAGCTGPKHSDCLACLFHNSGICELHCPA LVTYNTDTFESMPNPEGRTYFGASCVTACPYNYLSTDVGSCTLVC PLHNQEVTAEDGTQRCEKCSKPCARVCYGLGMEHLREVRVTSAN IQEFAGCKKIFGSLAFLPESFDGDPASNTAPLQPEQLQVFETLEE ITGYLYISAWPDSLPLSVFQNLQVIRGRILHNGAYSLTLQGLGI SWLGLRSLRELGSGLALIHNNTHLCFVHTVPWDQLFRNPHQALLH TANRPEDECVGEGLACHQLCARGHCWGPPTQCVNCSQFLRGQEC VEECRVLQGLPREYVNARHCLPCHPECQPQNGSVTCFGPEADQCV ACAHYKDPFPCVARCPGSKPDLSYMPIWKFPDEEGACQPCPINC THSCVDLDDKGCPAEQRASPLTSIIISAVVGILLVVVLGVVFGILII KRRQQKIRKYTMRRLLQETELVEPLTPSGAMPNQAQMRILKETEL RKVKVLGSGAFGTVYKGIWIPDGENVKIPVAIKVLENTSPKANK EILDEAYVMAGVGSPPYVSRLLGICLTSTVQLVTQLMPYGCLLDHV RENRRGLGSQDLLNWCMIKAGMSYLEDVRLVHRDLAARNVLVKS PNHVKITDFGLARLLDIDETEHADGGKVPKWMALLESILRRRFT HQSDVWSYGVTVWELMTFGAKPYDGIIPAREIPDLLEKGERLPQPP ICTIDVYMIMVKCWMIDSECRPRFRELVSFESRMARDPQRFVVIQ NEDLGPASPLDSTFYRSLLEDDDMGDLVDAEYLVPPQQGFPCDP APGAGGMVHRRHRSSTRSGGDLTLGLEPSEEEAPRSPLAPSEG

mAb or constant domain	SEQ ID NO	Amino acid sequence
		AGSDVFDGDLGMGAAKGLQSLPTHDPSPLQRYSEDPTVPLPSETD GYVAPLTCSPQPEYVNQPDVRPQPSPREGPLPAARPAGATLERP KTLSPGKNGVVKDVFAGGAVENPEYLTPQGGAAPQPHPPAFSP AFDNLYYWDQDPPERGAPPSTFKGTPTAENPEYLGLDVPV
Human IgG1 constant domain	81	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPS NTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLM ISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVSVLTVQLHQLDNLGKEYCKVSNKALPAPIEKTISKAKGQ PREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVMEAL HNHYTQKSLSLSPGK
Human Fab constant domain	292	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPS NTKVDKKVEPKSC
Human kappa constant domain	82	RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN ALQSGNSQESVTEQDSKSTYLSSTLTLSKADYEKHKVYACEVT HQGLSSPVTKSFNRGEC
Human lambda constant domain	291	GQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKAD SSPVKAGVETTTTPSKQSNKYAASSYLSLTPEQWKSHKYSYSCQVT HEGSTVEKTVAPTECS

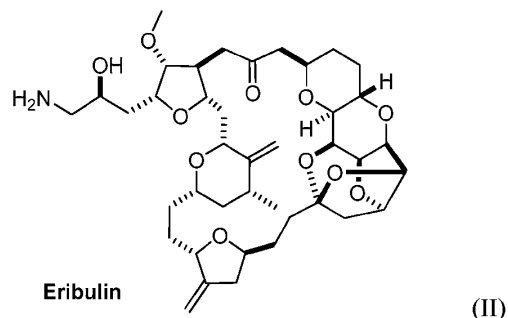
Drug Moieties

[00174] The drug moiety (D) of the ADCs and linker-payload conjugates described herein can be any chemotherapeutic agent. Useful classes of chemotherapeutic agents include, for example, anti-tubulin agents. In certain embodiments, the drug moiety is an anti-tubulin agent. One exemplary drug moiety for use in the described ADCs and linker-payload conjugates is eribulin.

[00175] Eribulin is a synthetic analog of the macrocyclic compound halichondrin B, which has been previously shown to be a potent inhibitor of tubulin polymerization, microtubule assembly, and tubulin-dependent GTP hydrolysis. Tubulin makes up dynamic filamentous cytoskeletal proteins called microtubules that are involved in a variety of vital cellular functions, including intracellular migration and transport, cell signaling, the maintenance of cell shape, and cell division. The rapid dividing rate of cancer cells makes them particularly sensitive to the obstruction of tubulin function. As such, halichondrin B and eribulin have

demonstrated notable anti-cancer activities *in vitro* and *in vivo* (Tan et al. (2009) Clin Cancer Res. 15(12): 4213-4219; Vahdat et al. (2009) J. Clin. Oncol. 27(18): 2954-2961). The mesylate salt of eribulin (eribulin mesylate) is currently marketed under the trade name Halaven™ for the treatment of patients with refractory metastatic breast cancer.

[00176] In various embodiments, the structure of eribulin used in its natural form in the disclosed ADCs and linker-payload conjugates is as shown in Formula (II):



[00177] In various other embodiments, the structure of the eribulin used in the disclosed ADCs and linker-conjugate payloads is as shown in Publ. No. US 20180193478, which is incorporated herein by reference for all eribulin structures and methods of synthesizing those structures.

Anti-eribulin Antibodies and Antigen-Binding Fragments

[00178] The present disclosure also provides antibodies or antigen-binding fragments thereof that specifically bind to eribulin, e.g., which may be used in any of the assays disclosed herein.

[00179] The antibodies disclosed herein that specifically bind eribulin may comprise three HC CDRs (HCDR1, HCDR2, and HCDR3) having amino acid sequences selected from the HC CDRs listed in Table 17, *infra*, as defined by the Kabat numbering system, and three light chain CDRs (LCDR1, LCDR2, and LCDR3) having amino acid sequences selected from the LC CDRs listed in Table 17, *infra*, as defined by the Kabat numbering system. In some embodiments, the antibodies comprise three heavy chain CDRs (HCDR1, HCDR2, and HCDR3) having amino acid sequences selected from the HC CDRs listed in Table 18, *infra*, as defined by the IMGT numbering system, and three light chain CDRs (LCDR1, LCDR2, and LCDR3) having amino acid sequences selected from the LC CDRs listed in Table 18, *infra*, as defined by the IMGT numbering system.

[00180] In some embodiments, an antibody disclosed herein comprises a VH domain having an amino acid sequence selected from SEQ ID NOs: 29, 101, 119, 137, 153, 169, 183, 200, 217, and 234 listed in Table 19, *infra*. In some embodiments, the antibody comprises a VL domain having an amino acid sequence selected from SEQ ID NOs: 30, 102, 120, 138, 154, 170, 184, 201, 218, and 235 listed in Table 19, *infra*.

[00181] In some embodiments, an antigen-binding fragment disclosed herein is a variant that retains eribulin binding specificity. In some embodiments, the antigen-binding fragment retains eribulin binding by comprising three heavy chain CDRs (HCDR1, HCDR2, and HCDR3) comprising amino acid sequences selected from the HC CDRs listed in Table 17, *infra*, as defined by the Kabat numbering system, and three light chain CDRs (LCDR1, LCDR2, and LCDR3) comprising amino acid sequences selected from the LC CDRs listed in Table 17, *infra*, as defined by the Kabat numbering system. In some embodiments, the antigen-binding fragment comprises three heavy chain CDRs (HCDR1, HCDR2, and HCDR3) comprising amino acid sequences selected from the HC CDRs listed in Table 18, *infra*, as defined by the IMGT numbering system, and three light chain CDRs (LCDR1, LCDR2, and LCDR3) comprising amino acid sequences selected from the LC CDRs listed in Table 18, *infra*, as defined by the IMGT numbering system. In some embodiments, the antigen-binding fragments disclosed herein may retain eribulin binding by comprising a VH domain comprising an amino acid sequence selected from SEQ ID NOs: 29, 101, 119, 137, 153, 169, 183, 200, 217, and 234 listed in Table 19, *infra*, and a VL domain comprising an amino acid sequence selected from SEQ ID NOs: 30, 102, 120, 138, 154, 170, 184, 201, 218, and 235 listed in Table 19, *infra*.

[00182] In some embodiments, an antibody or antigen-binding fragment further comprises human heavy and light chain frameworks (optionally with one or more backmutations to improve binding affinity) and/or human heavy and light chain constant domains or fragments thereof. For instance, the antibody or antigen-binding fragment may comprise a human IgG heavy chain constant domain (such as an IgG1) and a human kappa or lambda light chain constant domain. In some embodiments, the antibody or antigen-binding fragment comprises a human IgG1 heavy chain constant domain with a human Ig kappa light chain constant domain.

[00183] In some embodiments, an antibody that specifically binds eribulin comprises a heavy chain having an amino acid sequence selected from SEQ ID NOs: 31, 103, 121, 139,

155, 171, 185, 202, 219, and 236 listed in Table 20, *infra*. In some embodiments, an antibody that specifically binds eribulin comprises a light chain having an amino acid sequence selected from SEQ ID NOs: 32, 104, 122, 140, 156, 172, 186, 203, 220, and 237 listed in Table 20, *infra*.

[00184] Amino acid and nucleic acid sequences of exemplary anti-eribulin antibodies of the present disclosure, e.g., those which may be used in any of the assays disclosed herein, are set forth in Tables 17-21.

Table 17. Amino acid sequences of Kabat CDRs for anti-eribulin antibodies

mAb	IgG chain	SEQ ID	Amino acid sequence
5E4	HC CDR1	17	SSYGLC
	HC CDR2	18	CIYAGSSGLTYANWAKG
	HC CDR3	19	SLVGDGSGYGWYKL
	LC CDR1	20	QASQSVYKKNWLA
	LC CDR2	21	DASKLAS
	LC CDR3	22	AGGYDCSSADCNA
1L5	HC CDR1	89	SYGIC
	HC CDR2	90	CIGNSGSGSTYYASWAKG
	HC CDR3	91	SLYGDVSGYNWYRL
	LC CDR1	92	QASQSVYSNNYLS
	LC CDR2	93	GASTLAS
	LC CDR3	94	LGGYDCTSGDCNV
5E24	HC CDR1	107	STYYMC
	HC CDR2	108	GIDTGSLGISHYASWAKG
	HC CDR3	109	DAYS PDGVRGYAFGNFDL
	LC CDR1	110	QSSQSVWDNKNLA
	LC CDR2	111	SASTLAS
	LC CDR3	112	LGSYDYSRADCRA
5P14	HC CDR1	125	TSYHMC
	HC CDR2	126	CIYTSSDITWYANWAKG
	HC CDR3	127	GTGITDWSFNL

mAb	IgG chain	SEQ ID	Amino acid sequence
	LC CDR1	128	QASQNINSWLA
	LC CDR2	129	RASTLAS
	LC CDR3	130	QSNYYDSSSGSYGWS
6A12	HC CDR1	143	SNHHMC
	HC CDR2	144	CIYTIINITWYASWAKG
	HC CDR3	145	GAGSTDWSFNL
	LC CDR1	146	QASQSISSWLA
	LC CDR2	129	RASTLAS
	LC CDR3	147	QSNYYDGSSSYGWA
6K13	HC CDR1	159	SSYWIC
	HC CDR2	160	CMYNGDGSTYYASWAKG
	HC CDR3	161	NNNGYHFGL
	LC CDR1	162	QASQSVYNNNALS
	LC CDR2	21	DASKLAS
	LC CDR3	163	AGADLSVSDTYA
8E8	HC CDR1	175	GSYYMC
	HC CDR2	176	GIDTGSVGI SHYASWAKG
	HC CDR3	109	DAYS PDGVRGYAFGNFDL
	LC CDR1	177	QSSQSVWNNKHLA
	LC CDR2	111	SASTLAS
	LC CDR3	178	LGSYDYSSADCRA
9H3	HC CDR1	189	SNAMC
	HC CDR2	190	CIVNGDGYTTYASWVNG
	HC CDR3	191	SLVGDVSGYGWYDL
	LC CDR1	192	QSSQSVYGNNYLS
	LC CDR2	193	SASSLAS
	LC CDR3	194	LGGYDCSSDCNV
12M17	HC CDR1	206	NYWMC
	HC CDR2	207	CIYNGNVRPPYATWAKG
	HC CDR3	208	DSIFGDWDPFNL

mAb	IgG chain	SEQ ID	Amino acid sequence
	LC CDR1	44	QASQSVYSNNYLA
	LC CDR2	209	YASTLAS
	LC CDR3	210	QGGYDCSSVDCVA
12L15	HC CDR1	223	NSYWIC
	HC CDR2	224	CIYAGSSGSTYYPTWATG
	HC CDR3	225	GRDYDQGQYGAFGFAYYGLDL
	LC CDR1	226	QSSSVYKYKNWLS
	LC CDR2	227	GASNLAS
	LC CDR3	228	AGAYMIGTGPPFA

Table 18. Amino acid sequences of IMGT CDRs for anti-eribulin antibodies

mAb	IgG chain	SEQ ID	Amino acid sequence
5E4	HC CDR1	23	GFSFSSSYG
	HC CDR2	24	IYAGSSGLT
	HC CDR3	25	ARSLVGDGSGYGWYKL
	LC CDR1	26	QSVYKKNW
	LC CDR2	27	DAS
	LC CDR3	28	AGGYDCSSADCNA
1L5	HC CDR1	95	GFTLSSYG
	HC CDR2	96	IGNSGSGT
	HC CDR3	97	SRSLYGDVSGYNWYRL
	LC CDR1	98	QSVYSNNY
	LC CDR2	99	GAS
	LC CDR3	100	LGGYDCTSGDCNV
5E24	HC CDR1	113	GFSFSSTYY
	HC CDR2	114	IDTGLGIS
	HC CDR3	115	ARDAYSPDGVRGYAFGNFDL
	LC CDR1	116	QSVWDNKN
	LC CDR2	117	SAS
	LC CDR3	118	LGSYDYSRADCRA

mAb	IgG chain	SEQ ID	Amino acid sequence
5P14	HC CDR1	131	GFSESTSYH
	HC CDR2	132	IYTSSDIT
	HC CDR3	133	ARGTGITDWSFNL
	LC CDR1	134	QNINSW
	LC CDR2	135	RAS
	LC CDR3	136	QSNYYDSSSGSYGWS
6A12	HC CDR1	148	GFSESSNHH
	HC CDR2	149	IYTIINIT
	HC CDR3	150	VRGAGSTDWSFNL
	LC CDR1	151	QSISSW
	LC CDR2	135	RAS
	LC CDR3	152	QSNYYDGSSSYGWA
6K13	HC CDR1	164	GFSESSSYW
	HC CDR2	165	MYNGDGST
	HC CDR3	166	ARNNNGYHFGL
	LC CDR1	167	QSVYNNNA
	LC CDR2	27	DAS
	LC CDR3	168	AGADLSVSDTYA
8E8	HC CDR1	179	GFSESGSY
	HC CDR2	180	IDTGSVGIS
	HC CDR3	115	ARDAISPdGVRGYAFGNFDL
	LC CDR1	181	QSVWNNKH
	LC CDR2	117	SAS
	LC CDR3	182	LGSYDYSSADCRA
9H3	HC CDR1	195	GFDFSSNA
	HC CDR2	196	IVNGDGYT
	HC CDR3	197	ARSLVGDVSGYGWYDL
	LC CDR1	198	QSVYGNNY
	LC CDR2	117	SAS
	LC CDR3	199	LGGYDCSSDCNV

mAb	IgG chain	SEQ ID	Amino acid sequence
12M17	HC CDR1	211	GFTLNNYW
	HC CDR2	212	IYNGNVRP
	HC CDR3	213	VRDSIFGDWDPFNL
	LC CDR1	214	QSVYSNNY
	LC CDR2	215	YAS
	LC CDR3	216	QGGYDCSSVDCVA
12L15	HC CDR1	229	GFSEFSNSYW
	HC CDR2	230	IYAGSSGST
	HC CDR3	231	ARGRDYYDGQYGAFGFAYYGLDL
	LC CDR1	232	VSVYKYNW
	LC CDR2	99	GAS
	LC CDR3	233	AGAYMIGTGPFPA

Table 19. Amino acid sequences of variable regions for anti-eribulin antibodies

mAb	IgG chain	SEQ ID	Amino acid sequence
5E4	VH	29	QEQLLEESGGDLVKPEGSLTLTCTASGFSFSSSYGLCW VRQAPGKGLEWIACIYAGSSGLTYANWAKGRFTISK TSSTTVTLQMTSLTAADTATYFCARSLVGDGSGYGWY KLWGPGLTVTVSS
	VL	30	AQVLTQTASPVSAAVGGTVTINCQASQSVYKKNWLAW FQQKPGQPPKQLIYDASKLASGVSSRFSGSGSGTQFT LTISDVQCEDAATYYCAGGYDCSSADCNAGGGTEVV VK
1L5	VH	101	QEQLLEESGGDLVKPEGSLTLSCASGFTLSSYGICWV RQAPGKGPEWIAICIGNSGSTYYASWAKGRFTVSKTS STTVTLQMTSLTAADTATYFCSRSLYGDVSGYNWYRL WGPGLTVTVSS
	VL	102	AQVLTQTTSFVSAAVGGTVTINCQASQSVYSNNYLSW FQQKPGQPPKQLIYGASTLASGVPSRFKSGSGTQFT LTISDVQCADAATYYCLGGYDCTSGDCNVFGGGTEVV VK

mAb	IgG chain	SEQ ID	Amino acid sequence
5E24	VH	119	QSLEESGGDLVKPGASLTLTCTASGFSFSSTYYMCWV RQAPGKGLEWIGIDTGS LGISHYASWAKGRFTISK SSTTVTLQMTSLTAADTATYFCARDAYSPDGVRGYAF GNFDLWGPGLVTVSS
	VL	120	AQVLTQTASPVSAAVGSTVTINCQSSQSVWDNKNLAW FQQKPGQPPKRLIYASTLASGVSSRFKSGSGTQFT LTISGVQCDDAATYYCLGSYDYSRADCRAFGGGTEVV VK
5P14	VH	137	QEQLVESGGGLVQPEGSLTLTCTASGFSFSTSYHMCW VRQAPGKGLEWIGCIYTS SDITWYANWAKGRFTISKA SSTTVTLQMTSLTAADTATYFCARGTGITDWSFNLWG PGTLVTVSS
	VL	138	DIVMTQTPASVEAAVGGTVTIKCQASQNINSWLAWYQ QKPGQPPKLLIHRAS TLASGIPSRFRGSRSGTEYTLT ISDLECADAAATYYCQSNYYDSSSGSYGWSFGGGTEVV VK
6A12	VH	153	QEQLVESGGGLVQPEGSLTLTCTASGFSFSSNHHMCW VRQAPGKGLEWIGCIYTIINITWYASWAKGRFTISKA SSTTVTLQMTSLTAADTATLFCVRGAGSTDWSFNLWG PGTLVTVSS
	VL	154	DIVMTQTPASVEAAVGGTVTIKCQASQSISSWLAWYQ QKPGQPPKLLIYRASTLASGVPSRFKSGSGTQFTLT ISDLECADAAATYYCQSNYYDGSSSYGWAFGGGTEVV K
6K13	VH	169	QEQLVESGGDLVKPEGSLTLTCTASGFSFSSSYWICW VRQAPGKRPEWIA CMYNGDGSTYYASWAKGRFTISK SSTTVTLQMTSLTAADTATYFCARNNGYHFGWLWGP GLVTVSS
	VL	170	AAVLTQTASPVSAVGGTVTISCQASQSVYNNALSW FQQKVGQPPKVLIDASKLASGVPSRFSGSGSGTQFT LTISDVQCDDAATYYCAGADLSVSDTYAFGGGTEVV K
8E8	VH	183	QSLEESGGDLVKPGASLTLTCTASGFSFSGSYMCWV RQAPGKGLEWIGIDTGS VGISHYASWAKGRFTISK SSTTVTLQMTSLTAADTATYFCARDAYSPDGVRGYAF GNFDLWGPGLVTVSS

mAb	IgG chain	SEQ ID	Amino acid sequence
	VL	184	AQVLQTASPVSAAVGSTVTINCQSSQSVWNNKHLAW YQQKPGQPPKRLIYSASTLASGVSSRFRSGSGTHFT LTINDVQCDDAATYYCLGSYDYSSADCRAFGGGTEVV VK
9H3	VH	200	QEQLVESGGGLVQPGGSLTLTCKASGFDFSSNAMCWV RQAPGKGPWEIACIVNGDGYTYASWVNGRFTISRST SLNTVTLQMTSLTAADTATYFCARSLVGDVSGYGWYD LWGPGLTVTVSS
	VL	201	AAVVTQTPSSVSAAVGGTVSISCQSSQSVYGNLYLSW FQQKPGQPPKRLMYSASSLASGVPSRFSGSGSGTQFT LTISDVQCDDAATYYCLGGYDCSSDCNVFGGGTEVV K
12M17	VH	217	QSLEESGGGLVKPEGSLTLTCTASGFTLNMYWMCWVR QAPGKGLEWIGCIYNGNVRPYATWAKGRFTISKTS TTVTLQMTSLTAADTATYFCVRDSIFGDWDPFNLWGP GTLTVTVST
	VL	218	AQVLQTTPASVSAAVGGTVTINCQASQSVYSNNYLAW YQQKPGQPPKRLIYYASTLASGVPSRFKSGSGGTQFT LTISDVQCDDAATYYCQGGYDCSSVDCVAFGGGTEVV VK
12L15	VH	234	QEQLVESGGDLVKPEGSLTLTCTASGFSSFSNYSYICW VRQAPGKGLEWIAICYAGSSGLTYPTWATGRFVISK TSSTTVTLQMTSLTAADSGLYFCARGRDYYDQYGA GFAYYGLDLWGPGLTVTVSS
	VL	235	AAVLTQTTSPVSAAVGGTVTINCQSSSVYKYNWLSW YQQKPGQPPKLLIYGASNLASGVPSRFSGSGSGTQFT LTISAVQCDDAATYYCAGAYMIGTGPFPAFGGGTEVV VQ

Table 20. Amino acid sequences of full-length and Fab fragment antibody chains for anti-eribulin antibodies

mAb	IgG chain	SEQ ID	Amino acid sequence
5E4	Heavy chain	31	QEQLVESGGDLVKPEGSLTLTCTASGFSSFSYGLCW VRQAPGKGLEWIAICYAGSSGLTYANWAKGRFTISK TSSTTVTLQMTSLTAADTATYFCARSLVGDGSGYGWY KLWGPGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAA LGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG

mAb	IgG chain	SEQ ID	Amino acid sequence
			LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKV EPKSC
	Light chain	32	AQVLTQTASPVSAAVGGT VTINCQASQSVYKKNWLAW FQQKPGQPPKQLIYDASKLASGVSSRFSGSGSGTQFT LTISDVQCEDAATYYCAGGYDCSSADCNAGGGTEVV VKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPR EAKVQWKVDNALQSGNSQESVTEQDSKDSITYSLSTL TLISKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
5E4 (Alternative, IgG constant domain, heavy chain)	Heavy chain	294	QEQLSESGDLVKPEGS LTLTCTASGFSESSSYGLCW VRQAPKGLEWIA CIYAGSSGLTYANWAKGRFTISK TSSTTVTLQMTSLTAADTATYFCARSLVGDGSGYGWY KLWGPGLVTVSSASTKGPSVFPLAPSSKSTSGGTAA LGCLVKDYFPEPVT VSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKV EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLM ISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKT KPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQV SLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDS DGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYT QKSLSLSPGK
1L5	Heavy chain	103	QEQLSESGDLVKPEGS LTLCKASGFTLSSYGICWV RQAPKGPEWIA CIGNSGSSTYYASWAKGRFTVSKTS STTVTLQMTSLTAADTATYFCRSRLYGDVSGYNWYRL WGPGLVTVSSASTKGPSVFPLAPSSKSTSGGTAAAG CLVKDYFPEPVT VSWNSGALTSGVHTFPAVLQSSGLY SLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEP KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMIS RTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKP REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL PAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSG SFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQK SLSLSPGK
	Light chain	104	AQVLTQTTSFVSAAVGGT VTINCQASQSVSYNNYLSW FQQKPGQPPKQLIYGASTLASGVPSRFKSGSGTQFT LTISDVQCADAATYYCLGGYDCTSGDCNVFGGGTEVV VKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPR

mAb	IgG chain	SEQ ID	Amino acid sequence
			EAKVQWKVDNALQSGNSQESVTEQDSKDYSLSSSTL TLISKADYKHKVYACEVTHQGLSSPVTKSFNRGEC
5E24	Heavy chain	121	QSLLEESGGDLVKPGASLTLTCTASGFSFSSTYYMCWV RQAPGKGLEWITAGIDTGSGLGISHYASWAKGRFTISK SSTTVTLQMTSLTAADTATYFCARDAYS PDGVRGYAF GNFDLWGPGLTVTVSSASTKGPSVFPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ SSGLYSLSSVTVFSSSLGTQTYICNVNHKPSNTKVD KKVEPKSCDKHTCTCPPCPAPELLGGPSVFLFPPKPKD TLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHN AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPV LDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHN HYTQKSLSLSPGK
	Light chain	122	AQVLTQTASPVSAAVGSTVTINCQSSQSVWDNKNLAW FQQKPGQPPKRLIYSASTLASGVSSRFKSGSGTQFT LTISGVQCDDAATYYCLGSYDYSRADCFRGGGTEVV VKRTVAAPSVFIFPPSDEQLKSGTASVVCCLNNFYPR EAKVQWKVDNALQSGNSQESVTEQDSKDYSLSSSTL TLISKADYKHKVYACEVTHQGLSSPVTKSFNRGEC
5P14	Heavy chain	139	QEQLVESGGGLVQPEGLSLTLCTASGFSFSTSYHMCW VRQAPGKGLEWIGCIYTSSDITWYANWAKGRFTISKA SSTTVTLQMTSLTAADTATYFCARGTGITDWSFNLWG PGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCL VKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSL SSVTVFSSSLGTQTYICNVNHKPSNTKVDKKVEPKS CDKHTCTCPPCPAPELLGGPSVFLFPPKPKDTLMISRT PEVTCVVDVSHEDPEVKFNWYVDGVEVHNNAKTKPRE EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCL LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF FLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSL SLSPGK
	Light chain	140	DIVMTQTPASVEAAVGGTVTIKQASQNINSWLAWYQ QKPGQPPKLLIHRASTLASGIPSRFRGSRSGTEYTLT ISDLECAATAATYYCQSNYYDSSSGSYGWSFGGGTEVV VKRTVAAPSVFIFPPSDEQLKSGTASVVCCLNNFYPR

mAb	IgG chain	SEQ ID	Amino acid sequence
			EAKVQWKVDNALQSGNSQESVTEQDSKDYSLSTL TLKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
6A12	Heavy chain	155	QEQLVESGGGLVQPEGSLTLTCTASGFSSNNHMCW VRQAPGKGLEWIGCIYTIINITWYASWAKGRFTISKA SSTTVTLQMTSLTAADTATLFCVRGAGSTDWSFNLWG PGTLTVVSSASTKGPSVFPLAPSSKSTSGGTAALGCL VKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSL SSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKS CDKHTCTPPCPAPELLGGPSVFLFPPKPKDTLMISRT PEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTC LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF FLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSL SLSPGK
	Light chain	156	DIVMTQTPASVEAAVGGTVTIKQASQSISSWLAWYQ QKPGQPPKLLIYRASTLASGVPSRFKSGSGTQFTLT ISDLECAATAATYYCQSNYYDGSSSYGWAFFGGTEVVV KRTVAAPSVEIFPPSDEQLKSGTASVCLLNNFYPRE AKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
6K13	Heavy chain	171	QEQLVESGGDLVKPEGSLTLTCTASGFSSSYWICW VRQAPGKRPEWIACMYNGDGSYYASWAKGRFTISKT SSTTVTLQMTSLTAADTATYFCARNNGYHFGWLWPG TLTVVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVK DYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSS VVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD KHTCTPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQ YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL YSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSL SPGK
	Light chain	172	AAVLTQTASPVSAFVGGTVTISCQASQSVYNNALSW FQQKVGQPPKVLIIYDASKLASGVPSRFSGSGSGTQFT LTISDVQCDDAATYYCAGADLSVSDTYAFGGTEVVV KRTVAAPSVEIFPPSDEQLKSGTASVCLLNNFYPRE

mAb	IgG chain	SEQ ID	Amino acid sequence
			AKVQWKVDNALQSGNSQESVTEQDSKDYSLSSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
8E8	Heavy chain	185	QSLLESGGDLVKPGASLTLTCTASGFSFSGSYMCWV RQAPGKGLEWIAIDTGSVGIASHYASWAKGRFTISK SSTTVTLQMTSLTAADTATYFCARDAYS PDGVRGYAF GNFDLWGPGLVTVSSASTKGPSVFPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ SSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVD KKVEPKSCDKHTCTPCPAPELLGGPSVFLFPPKPKD TLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHN AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPV LDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHN HYTQKSLSPGK
	Light chain	186	AQVLTQTASPVSAAVGSTVTINCQSSQSVWNNKHLAW YQQKPGQPPKRLIYASSTLASGVSSRFRGSGSGTHFT LTINDVQCDDAATYYCLGSYDYSSADCRAFGGGTEVV VKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPR EAKVQWKVDNALQSGNSQESVTEQDSKDYSLSSSTL T LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
9H3	Heavy chain	202	QEQLVESGGGLVQPGGSLTLTCKASGFDFSSNAMCWV RQAPGKGP EWIAICIVNGDGYTYASWVNGRFTISRST SLNTVTLQMTSLTAADTATYFCARSLVGDVSGYGWYD LWGPGLVTVSSASTKGPSVFPLAPSSKSTSGGTAAL GCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL YSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVE PKSCDKHTCTPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNATK PREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKA LPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVS LTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSD GSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQ KSLSPGK
	Light chain	203	AAVVTQTPSSVSAAVGGTVSISCQSSQSVYGNLYLSW FQQKPGQPPKRLMYSASSLASGVPSRFRGSGSGTQFT LTISDVQCDDAATYYCLGGYDCSSDCNVFGGGTEVVV KRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPRE

mAb	IgG chain	SEQ ID	Amino acid sequence
			AKVQWKVDNALQSGNSQESVTEQDSKDYSLSSLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
12M17	Heavy chain	219	QSLLEESGGGLVKPEGSLLTCTASGFTLNYYWMCWVR QAPGKGLEWIGCIYNGNVRPYATWAKGRFTISKSS TTVTLQMTSLTAADTATYFCVRDSIFGDWDPFNLWGP GTLTVSTASTKGPSVFPLAPSSKSTSGGTAALGCLV KDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSL SVVTVFSSSLGTQTYICNVNHKPSNTKVDKKVEPKSC DKTHCTCPCPAPELLGGPSVFLFPPKPKDTLMISRT EVTCTVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE QYNSTYRVVSVLTVHLQDNLNGKEYKCKVSNKALPAP IEKTIKAKGQPREPQVYTLPPSRDELTKNQVSLTCL VKGFYPSDIAVEWESNGQPENNYKTTPVLDSDGSFF LYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLS LSPGK
	Light chain	220	AQVLTQTPASVSAVGGTVTINCQASQSVYSNNYLAW YQQKPGQPPKRLIYYASTLASGVPSRFKSGSGTQFT LTISDVQCDDAATYYCQGGYDCSSVDCVAFGGGTEVV VKRTVAAPSVFIFPPSDEQLKSGTASVVCCLNNFYPR EAKVQWKVDNALQSGNSQESVTEQDSKDYSLSSLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
12L15	Heavy chain	236	QEQLLEESGGDLVKPEGSLLTCTASGFSSNSYWICW VRQAPGKGLEWIIACIYAGSSGSTYYPTWATGRFVISK TSSTVTTLQMTSLTAADSGLYFCARGRDYYDQYGA GFAYYGLDLWGPGTLTVSSASTKGPSVFPLAPSSKS TSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTF AVLQSSGLYSLSSVTVFSSSLGTQTYICNVNHKPSN TKVDKKVEPKSCDKTHCTCPCPAPELLGGPSVFLFPP KPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYNSTYRVVSVLTVHLQDNLNGKEY KCKVSNKALPAPIEKTIKAKGQPREPQVYTLPPSRD ELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHE ALHNHYTQKSLSLSPGK
	Light chain	237	AAVLTQTTSPVSAVGGTVTINCQSSVSVKYNWLSW YQQKPGQPPKLLIYGASNLASGVPSRFSGSGSGTQFT LTISAVQCDDAATYYCAGAYMIGTGPFFAFGGGTEVV VQRTVAAPSVFIFPPSDEQLKSGTASVVCCLNNFYPR

mAb	IgG chain	SEQ ID	Amino acid sequence
			EAKVQWKVDNALQSGNSQESVTEQDSKSTYSLSSL TLISKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

Table 21. Nucleic acid sequences of full-length antibody chains for anti-eribulin antibodies

mAb	IgG chain	SEQ ID	Nucleic acid sequence
5E4	Heavy chain	85	CAGGAGCAGCTGGAGGAGTCCGGGGGAGACCTGGTCAAGCCTGAGGG ATCCCTGACACTCACCTGCACAGCCTCTGGATTCTCCTTCAGTAGCA GCTACGGGTTATGTTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAG TGGATCGCATGCATTTATGCTGGTAGTAGTGGTCTCACTTACTACGC GAACTGGGCGAAAGGCCGATTACCATCTCCAAAACCTCGTCGACCA CGGTGACTCTGCAAATGACAGTCTGACAGCCGCGACACGGCCACC TATTTCTGTGCGAGATCTCTTGTGGTGATGGTAGTGGTTATGGTTG GTATAAGTTGTGGGGCCAGGCACCCCTGGTCACCGTCTCCTCAGCAT CCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCCTCCTCAAGAGC ACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTT CCCCGAACCGGTGACGGTGTCTGTGGAACCTAGGCGCCCTGACCAGCG GCGTGCACACCTTCCCGGCTGTCTACAGTCTCAGGACTCTACTCC CTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGAC CTACATCTGCAACGTGAATCACAAGCCAGCAACACCAAGGTGGACA AGAAAGTTGAGCCCAAATCTTGTGACAAAACCTCACACATGCCACCG TGCCCAGCACCTGAACCTCCTGGGGGGACCGTCAGTCTTCTCTTCCC CCCAAAACCAAGGACACCCCTCATGATCTCCCGGACCCCTGAGGTCA CATGCGTGGTGGTGGACGTGAGCCACGAAGACCTGAGGTCAAGTTC AACTGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCC GCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCTCTCA CCGTCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAG GTCTCCAACAAAGCCCTCCAGCCCCCATCGAGAAAACCATCTCCAA AGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCTGCCCCCAT CCCGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTC AAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGG GCAGCCGGAGAACAACCTACAAGACCACGCCTCCCGTGTGACTCCG ACGGCTCCTTCTTCTTATATTCAAAGCTCACCGTGGACAAGAGCAGG TGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCT GCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCCGGGAAA
	Light chain	86	GCCCAAGTGCTGACCCAGACTGCATCGCCGTGTCTGCAGCTGTGGG AGGCACAGTCACCATCAATTGCCAGGCCAGTCAGAGTGTTTATAAGA AGAACTGGTTAGCCTGGTTTCAGCAGAAACCAGGGCAGCCTCCAAA

mAb	IgG chain	SEQ ID	Nucleic acid sequence
			CAACTGATCTATGATGCATCGAACTGGCATCTGGGGTCTCATCGCG GTTCAGCGGCAGTGGATCTGGGACACAGTTCACCTCTCACCATCAGCG ACGTGCAGTGCGAAGATGCTGCCACTTACTACTGTGCAGGCGGTTAT GATTGTAGTAGTGCTGATTGTAATGCTTTCGGCGGAGGGACCGAGGT GGTGGTCAAACGAACTGTGGCTGCACCATCTGTCTTCATCTTCCCGC CATCTGATGAGCAGTTGAAATCTGGAAGTGCCTCTGTTGTGTGCCTG CTGAATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGAAGGTGGA TAACGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTACAGAGCAGG ACAGCAAGGACAGCACCTACAGCCTCAGCAGCACCTGACGCTGAGC AAAGCAGACTACGAGAAACACAAAGTCTACGCTGCGAAGTCACCCA TCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGAGAGT GT
IL5	Heavy chain	105	CAGGAGCAGCTGGAGGAGTCCGGGGGAGACCTGGTCAAGCCTGAGGG ATCCCTGACACTCTCCTGCAAAGCCTCTGGATTACCCCTCAGTAGCT ACGGGATATGTTGGGTCCGCCAGGCTCCAGGGAAGGGGCTTGAGTGG ATCGCGTGCATTGGTAATGGTAGTGGTAGCACTTACTACGCGAGCTG GGCGAAAGGCCGATTACCGTCTCCTCAAAACCTCGTCGACCACGGTGA CTCTGCAAATGACCAGTCTGACAGCCGCGGACACGGCCACCTATTTT TGTTTCGAGATCTCTTTATGGTGATGTTAGTGGTTATAATTGGTATAG ATTGTGGGGCCAGGCACCTGGTCACCGTCTCCTCAGCATCCACCA AGGGCCCATCGGTCTTCCCCCTGGCACCTCTCTCAAGAGCACCTCT GGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGA ACCGGTGACGGTGTCTGTGGAAGTCAAGCGCCCTGACCAGCGGCGTGC ACACCTTCCCGGCTGTCTTACAGTCTCAGGACTCTACTCCCTCAGC AGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACAT CTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGAAAG TTGAGCCCAAATCTTGTGACAAAACCTCACACATGCCACCGTGCCCA GCACCTGAACTCCTGGGGGGACCGTCAGTCTTCTCTTCCCCCAA ACCCAAGGACACCTCATGATCTCCGGACCCCTGAGGTACATGCG TGGTGGTGGACGTGAGCCACGAAGACCTGAGGTCAAGTCAAGTGG TACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGA GGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCTCACCCTCC TGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGAAGGTCTCC AACAAAGCCCTCCAGCCCCATCGAGAAAACATCTCCAAGCCAA AGGGCAGCCCCGAGAACCACAGGTGTACACCTGCCCCCATCCGGG ATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGC TTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCC GGAGAACAACCTACAAGACCACGCTCCCGTGTGGACTCCGACGGCT

mAb	IgG chain	SEQ ID	Nucleic acid sequence
			CCTTCTTCTTATATTCAAAGCTCACCGTGGACAAGAGCAGGTGGCAG CAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAA CCACTACACGCAGAAGAGCCTCTCCCTGTCTCCCGGAAA
	Light chain	106	GCCCAAGTGCTGACCCAGACTACATCGCCCGTGTCTGCAGCTGTGGG AGGCACAGTCACCATCAATTGCCAGGCCAGTCAGAGTGTTTATAGTA ACAACTACTTATCTGGTTTCAGCAGAAACCAGGGCAGCCTCCCAAG CAACTGATCTATGGTGCATCCACTCTGGCATCTGGGGTCCCATCGCG GTTCAAAGGCAGTGGATCTGGGACACAGTTCACTCTCACCATCAGCG ACGTGCAGTGTGCCGATGCTGCCACTTACTACTGTCTAGGCGGTTAT GATTGTACTAGTGGTGATTGTAATGTTTTCGGCGGAGGGACCGAGGT GGTGGTCAAACGAACGTGGCTGCACCATCTGTCTTCATCTTCCCGC CATCTGATGAGCAGTTGAAATCTGGAACGCTCTGTGTGTGCGCTG CTGAATAACTTCTATCCAGAGAGGCCAAAGTACAGTGGAAGGTGGA TAACGCCCTCCAATCGGGTAACTCCAGGAGAGTGTACAGAGCAGG ACAGCAAGGACAGCACCTACAGCCTCAGCAGCACCTGACGCTGAGC AAAGCAGACTACGAGAAACACAAAGTCTACGCCTGCGAAGTCACCCA TCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGAGAGT GT
5E24	Heavy chain	123	CAGTCGTGGAGGAGTCCGGGGGAGACCTGGTCAAGCCTGGGGCGTC CCTGACACTCACCTGCACAGCCTCTGGATTCTCCTTCAGTAGTACCT ACTACATGTGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGG ATCGCTGGCATTGATACTGGTAGTCTTGGTATCAGTCACTACGCGAG CTGGGCGAAAGGCCGATTACCATCTCCAAAACCTCGTCGACCACGG TGACTCTGCAAATGACCAGTCTGACAGCCGCGGACACGGCCACCTAT TTCTGTGCGAGAGACGCTTACTCACCTGATGGTGTTCGTGGTTATGC TTTTGGTAACTTTGACTTGTGGGGCCAGGCACCCTGGTCACTGTCT CCTCAGCATCCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCCTCC TCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCGTGGTCAA GGACTACTTCCCCGAACCGGTGACGGTGTCTGTGGAACCTCAGGCGCCC TGACCAGCGGCGTGACACCTTCCCGGCTGTCTACAGTCCTCAGGA CTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGG CACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCA AGGTGGACAAGAAAGTTGAGCCCAAATCTTGTGACAAAACTCACACA TGCCCACCGTGCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTT CCTCTTCCCCCAAACCCAAGGACACCCTCATGATCTCCCGGACCC CTGAGGTACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAG GTCAAGTTCAACTGGTACGTGGACGGCGTGAGGTGCATAATGCCAA GACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCA

mAb	IgG chain	SEQ ID	Nucleic acid sequence
			GCGTCCTCACCCTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTAC AAGTGCAAGGTCTCCAACAAAGCCCTCCAGCCCCATCGAGAAAAC CATCTCCAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCC TGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTGAGCTGACC TGCCTGGTCAAAGGCTTCTATCCAGCGACATCGCCGTGGAGTGGGA GAGCAATGGGCAGCCGGAGAACAATAAGACCACGCCTCCCGTGC TGGACTCCGACGGCTCCTTCTTCTATATTCAAAGCTCACCGTGGAC AAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCA TGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTC CCGGGAAA
	Light chain	124	GCCAAGTGCTGACCCAGACTGCATCGCCCGTGTCTGCAGCTGTGGG AAGCACAGTCACCATCAATTGCCAGTCCAGTCAGAGTGTGGGATA ACAAAAATTTAGCCTGGTTTCAGCAGAAACCAGGGCAGCCTCCCAAG CGCCTGATCTATTCTGCATCCACTCTGGCATCTGGGGTCTCATCGCG GTTCAAAGGCAGTGGATCTGGGACACAGTTCACTCTCACCATCAGCG GCGTGCAGTGTGACGATGCTGCCACTTACTACTGTCTAGGCAGTTAT GATTATAGCCGTGCTGATTGTAGAGCTTTCGGCGGAGGGACCGAGGT GGTGGTCAAACGAACGTGGCTGCACCATCTGTCTTCATCTTCCCGC CATCTGATGAGCAGTTGAAATCTGGAACGCTCTGTGTGTGCGCTG CTGAATAACTTCTATCCAGAGAGGCCAAAGTACAGTGAAGGTGGA TAACGCCCTCCAATCGGGTAACTCCAGGAGAGTGTACAGAGCAGG ACAGCAAGGACAGCACCTACAGCCTCAGCAGCACCTGACGCTGAGC AAAGCAGACTACGAGAAACACAAAGTCTACGCCTGCGAAGTCACCCA TCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGAGAGT GT
5P14	Heavy chain	141	CAGGAGCAGCTGGTGGAGTCCGGGGAGGCCTGGTCCAGCCTGAGGG ATCCCTGACACTCACCTGCACAGCTTCTGGATTCTCCTTCAGTACTA GCTATCACATGTGCTGGGTCCGCCAGGCTCCAGGGAAGGGCTGGAG TGGATCGGATGCATTTATACTAGTAGTGATATCACATGGTACGCGAA CTGGGCGAAAGGCCGATTACCATCTCCAAGGCCTCGTCGACCACGG TGACTCTGCAAATGACCAGTCTGACAGCCGCGGACACGGCCACCTAT TTCTGTGCGAGGGGGACTGGTATTACTGATTGGTCCTTTAACTTGTG GGGCCAGGCACCCTGGTCACCGTCTCCTCAGCATCCACCAAGGGCC CATCGGTCTTCCCCCTGGCACCTCCTCCAAGAGCACCTCTGGGGGC ACAGCGGCCCTGGGTGCTGGTCAAGGACTACTTCCCCGAACCGGT GACGGTGTCTGGAACCTAGGCGCCCTGACCAGCGCGTGCACACCT TCCCGGCTGTCTACAGTCTCTCAGGACTCTACTCCCTCAGCAGCGTG GTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAA

mAb	IgG chain	SEQ ID	Nucleic acid sequence
			CGTGAATCACAGCCCAGCAACACCAAGGTGGACAAGAAAGTTGAGC CCAAATCTTGTGACAAAACCTCACACATGCCACCGTGCCAGCACCT GAACTCCTGGGGGACCGTCAGTCTTCTCTTCCCCCAAACCCAA GGACACCCCTCATGATCTCCCGACCCCTGAGGTCACATGCGTGGTGG TGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTG GACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCA GTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACC AGGACTGGCTGAATGGCAAGGAGTACAAGTGAAGGTCTCCAACAAA GCCCTCCAGCCCCATCGAGAAAACCATCTCCAAGCCAAAGGGCA GCCCCGAGAACCACAGGTGTACACCTGCCCCATCCCGGGATGAGC TGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTAT CCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAA CAACTACAAGACCACGCCTCCCGTGTGGACTCCGACGGCTCCTTCT TCTTATATTCAAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGG AACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCTCCCGGAAA
	Light chain	142	GACATTGTGATGACCCAGACTCCAGCCTCCGTGGAGGCAGCTGTGGG AGGCACAGTCACCATCAAGTGCCAGGCCAGTCAGAACATTAATAGTT GGTTAGCCTGGTATCAGCAGAAACCAGGGCAGCCTCCCAAGCTCCTG ATCCACAGGGCATCCACTCTGGCATCTGGGATCCCATCGCGGTTTCAG AGGCAGTAGATCTGGGACAGAGTACACTCTCACCATCAGCGACCTGG AGTGTGCCGATGCTGCCACTTACTACTGTCAAAGCAATTATTATGAT AGTAGTAGTGGTAGTTATGGTTGGTCTTTCGGCGGAGGGACCGAGGT GGTCTGCAAACGAACGTGGCTGCACCATCTGTCTTCATCTTCCCGC CATCTGATGAGCAGTTGAAATCTGGAAGTGCCTCTGTTGTGTGCCTG CTGAATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGGA TAACGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTACAGAGCAGG ACAGCAAGGACAGCACCTACAGCCTCAGCAGCACCTGACGCTGAGC AAAGCAGACTACGAGAAACACAAAGTCTACGCTGCGAAGTCACCCA TCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGAGAGT GT
6A12	Heavy chain	157	CAGGAGCAGCTGGTGGAGTCCGGGGGAGGCCTGGTCCAGCCTGAGGG ATCCCTGACACTCACCTGCACAGCTTCTGGATTCTCCTTCAGTAGCA ATCACCACATGTGCTGGGTCCGCCAGGCTCCAGGGAAGGGACTGGAA TGGATCGGATGCATTTATACGATCATTAATATCACATGGTACGCGAG CTGGGCGAAAGGCCGATTACCATCTCCAAGGCCTCGTCGACCACGG TGAATCTGCAAATGACCAGTCTGACAGCCGCGGACACGGCCACCTTG TTCTGTGTGAGGGGGCTGGTAGTACTGATTGGTCCTTTAACTGTGTG

mAb	IgG chain	SEQ ID	Nucleic acid sequence
			GGGCCCAGGCACCCTGGTCACCGTCTCCTCAGCATCCACCAAGGGCC CATCGGTCTTCCCCCTGGCACCCCTCCTCCAAGAGCACCTCTGGGGGC ACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGT GACGGTGTCTGGAACCTAGGCGCCCTGACCAGCGCGCTGCACACCT TCCCGGCTGTCTACAGTCTCAGGACTCTACTCCCTCAGCAGCGTG GTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAA CGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGAAAGTTGAGC CCAAATCTTGTGACAAAACCTCACACATGCCCACCGTGCCACAGCCT GAACTCCTGGGGGGACCGTCAGTCTTCTCTTCCCCCAAACCCAA GGACACCCCTCATGATCTCCCGACCCCTGAGGTCACATGCGTGGTGG TGGACGTGAGCCACGAAGACCCCTGAGGTCAAGTTCAACTGGTACGTG GACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCA GTACAACAGCACGTACCGTGTGGTCAGCGTCTCACCCTCCTGCACC AGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAA GCCCTCCCAGCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCA GCCCCGAGAACCACAGGTGTACACCTGCCCCATCCCGGGATGAGC TGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTAT CCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAA CAACTACAAGACCACGCCCTCCCGTGTGGACTCCGACGGCTCTTCT TCTTATATTCAAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGG AACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTA CACGCAGAAGAGCCTCTCCCTGTCTCCCGGGAAA
	Light chain	158	GACATTGTGATGACCCAGACTCCAGCCTCCGTGGAGGCAGCTGTGGG AGGCACAGTCACCATCAAGTGCCAGGCCAGTCAGAGCATTAGCAGTT GGTTAGCCTGGTATCAGCAGAAACCAGGGCAGCCTCCCAAGCTCCTG ATCTACAGGGCATCCACTCTGGCATCTGGGGTCCCATCTCGGTTCAA AGGCAGTGGATCTGGGACACAGTTCACTCTCACCATCAGCGACCTGG AGTGTGCCGATGCTGCCACGTACTACTGTGTCAGAGCAATTATTATGAT GGTAGTAGTAGTTATGGTTGGGCTTTCGGCGGAGGGACCGAGGTGGT GGTCAAACGAACCTGTGGCTGCACCATCTGTCTTCATCTTCCCGCCAT CTGATGAGCAGTTGAAATCTGGAACCTGCCTCTGTTGTGTGCCTGCTG AATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTACAGAGCAGGACA GCAAGGACAGCACCTACAGCCTCAGCAGCACCTGACGCTGAGCAAA GCAGACTACGAGAAACACAAAGTCTACGCCTGCGAAGTCACCCATCA GGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGAGAGTGT
6K13	Heavy chain	173	CAGGAGCAGCTGGAGGAGTCCGGGGGAGACCTGGTCAAGCCTGAGGG ATCCCTGACACTCACCTGCACAGCCTCTGGATTCTCCTTCAGTAGCA

mAb	IgG chain	SEQ ID	Nucleic acid sequence
			GCTACTGGATATGCTGGGTCCGCCAGGCTCCAGGGAAGAGGCCTGAG TGGATCGCATGTCATGTATAATGGTGATGGCAGCACATACTACGCGAG CTGGGCGAAAGGCCGATTACCATCTCCAAAACCTCGTCGACCACGG TGACTCTGCAAATGACCAGTCTGACAGCCGCGGACACGGCCACTTAT TTCTGTGCGCGAAATAATAACGGCTACCATTTTGGCTTGTGGGGCCC AGGCACCCCTGGTCACCGTCTCCTCAGCATCCACCAAGGGCCCATCGG TCTTCCCCCTGGCACCCCTCCTCCAAGAGCACCTCTGGGGGCACAGCG GCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGT GTCGTGGAACCTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGG CTGTCTACAGTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACC GTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAA TCACAAGCCCAGCAACACCAAGGTGGACAAGAAAGTTGAGCCCAAAT CTTGTGACAAACTCACACATGCCCACCGTGCCAGCACCTGAACTC CTGGGGGGACCGTCAGTCTTCTCTTCCCCCAAACCCAAGGACAC CCTCATGATCTCCCGGACCCCTGAGGTACATGCGTGGTGGTGACG TGAGCCACGAAGACCCCTGAGGTCAAGTTCAACTGGTACGTGGACGGC GTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAA CAGCACGTACCGTGTGGTCAGCGTCTCACCCTCCTGCACCAGGACT GGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTC CCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGCAGCCCCG AGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCA AGAACCAGGTGAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCAGC GACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAATA CAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCTTAT ATTCAAAGCTCACCCTGGACAAGAGCAGGTGGCAGCAGGGGAACGTC TTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCA GAAGAGCCTCTCCCTGTCTCCCGGAAA
	Light chain	174	GCCGCCGTGCTGACCCAGACTGCATCTCCCGTGTCTGCACCTGTGGG AGGCACAGTCACCATCAGTTGCCAGGCCAGTCAGAGTGTTTATAATA ACAATGCCTTATCCTGGTTTCAGCAGAAAGTAGGGCAGCCTCCCAAG GTCCTGATCTATGATGCATCCAAACTGGCATCTGGGGTCCCATCGCG GTTCAGTGGCAGTGGATCTGGGACACAATTCACTCTCACCATCAGCG ACGTGCAGTGTGACGATGCTGCCACTTACTACTGTGCAGGCGCTGAT CTTAGTGTTAGTGATACGTATGCTTTCGGCGGAGGGACCGAGGTGGT GGTCAAACGAACTGTGGCTGCACCATCTGTCTTCATCTTCCGCCAT CTGATGAGCAGTTGAAATCTGGAAGTGCCTCTGTTGTGTGCCCTGCTG AATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTACAGAGCAGGACA

mAb	IgG chain	SEQ ID	Nucleic acid sequence
			GCAAGGACAGCACCTACAGCCTCAGCAGCACCTGACGCTGAGCAAA GCAGACTACGAGAAACACAAAGTCTACGCTGCGAAGTCACCCATCA GGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGAGAGTGT
8E8	Heavy chain	187	CAGTCGTTGGAGGAGTCCGGGGGAGACCTGGTCAAGCCTGGGGCATC CCTGACACTCACCTGCACAGCCTCTGGATTCTCCTTCAGTGGCAGCT ACTACATGTGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGG ATCGCTGGCATTGATACTGGTAGTGTAGGTATCAGTCACTACGCGAG CTGGGCGAAAGGCCGATTACCATCTCCAAAACCTCGTCGACCACGG TGACTCTGCAAATGACCAGTCTGACAGCCGCGGACACGGCCACCTAT TTCTGTGCGAGAGACGCTTACTCACCTGATGGTGTTCGTGGTTATGC TTTTGGTAACTTTGACTTGTGGGGCCAGGCACCCCTGGTCACCGTCT CCTCAGCATCCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCTCC TCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAA GGACTACTTCCCCGAACCGGTGACGGTGTCTGTGGAACCTCAGGCGCCC TGACCAGCGCGCTGCACACCTTCCCGGTGTCTACAGTCCTCAGGA CTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGG CACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCA AGGTGGACAAGAAAGTTGAGCCCAAATCTTGTGACAAAACACACA TGCCCCACCGTGCCAGCACCTGAACTCCTGGGGGACCGTCAGTCTT CCTCTTCCCCCAAACCCAAGGACACCCCTCATGATCTCCCGGACCC CTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCTGAG GTCAAGTTCAACTGGTACGTGGACGGCGTGAGGTGCATAATGCCAA GACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCA GCGTCCTCACCGTCTTGACACAGGACTGGCTGAATGGCAAGGAGTAC AAGTGCAAGGTCTCCAACAAAGCCCTCCAGCCCCATCGAGAAAAC CATCTCCAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCC TGCCCCCATCCCGGATGAGCTGACCAAGAACCAGGTACGCTGACC TGCTGGTCAAAGGCTTCTATCCAGCGACATCGCCGTGGAGTGGGA GAGCAATGGGCAGCCGAGAACTACAAGACCACGCTCCCGTGC TGGACTCCGACGGCTCCTTCTTCTTATATTCAAAGCTACCGTGGAC AAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCA TGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTC CCGGGAAA
	Light chain	188	GCCCAAGTGCTGACCCAGACTGCATCGCCGTGTGTCAGCTGTGGG AAGCACAGTCACCATCAATTGCCAGTCCAGTCAGAGTGTGGGAATA ACAAACATTTAGCCTGGTATCAGCAGAAACCAGGGCAGCCTCCCAAG CGCCTGATCTATTCTGCATCCACTCTGGCATCTGGGGTCTCATCGCG GTTTCAGAGGCAGTGGATCTGGGACACACTTCACTCTCACCATCAACG

mAb	IgG chain	SEQ ID	Nucleic acid sequence
			ACGTGCAGTGTGACGATGCTGCCACTTACTACTGTCTAGGCAGTTAT GATTACAGTAGTGCTGATTGTAGAGCTTTCGGCGGAGGGACCGAGGT GGTGGTCAAACGAACTGTGGCTGCACCATCTGTCTTCATCTTCCCGC CATCTGATGAGCAGTTGAAATCTGGAAGTGCCTCTGTTGTGTGCCTG CTGAATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGGA TAACGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTACAGAGCAGG ACAGCAAGGACAGCACCTACAGCCTCAGCAGCACCTGACGCTGAGC AAAGCAGACTACGAGAAACACAAAGTCTACGCCTGCGAAGTCAACCA TCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGAGAGT GT
9H3	Heavy chain	204	CAGGAGCAGCTGGTGGAGTCCGGGGGAGGCCTGGTCCAGCCTGGGGG ATCCCTGACACTCACCTGCAAAGCCTCTGGATTGCACTTCAGTAGCA ATGCAATGTGCTGGGTCCGCCAGGCTCCAGGAAGGGGCTGAGTGG ATCGCATGCATTGTTAATGGTGATGGCTACACATACTACGCGAGCTG GGTGAATGGCCGATTACCATCTCCAGAAGCACCAGCCTAAACACGG TGACTCTGCAAATGACCAGTCTGACAGCCGCGGACACGGCCACCTAT TTCTGTGCGAGATCTCTGTTGGTGATGTTAGTGGTTATGGTTGGTA TGACTTGTGGGGCCAGGCACCTGGTCACCGTCTCCTCAGCATCCA CCAAGGGCCCATCGGTCTTCCCCCTGGCACCTCCTCCAAGAGCACC TCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCC CGAACCAGGTGACGGTGTCTGTGAACTCAGGCGCCCTGACCAGCGCG TGCACACCTTCCCGGCTGTCTACAGTCCTCAGGACTCTACTCCCTC AGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTA CATCTGCAACGTGAATCACAAGCCAGCAACACCAAGGTGGACAAGA AAGTTGAGCCCAAATCTTGTGACAAAACCTCACACATGCCCACCGTGC CCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTTCTCTTCCCCC AAAACCAAGGACACCCTCATGATCTCCCGACCCCTGAGGTACAT GCGTGGTGGTGGACGTGAGCCACGAAGCCCTGAGGTCAAGTTCAAC TGGTACGTGGACGGCTGGAGGTGCATAATGCCAAGACAAAGCCGCG GGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCTCACC TCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTC TCCAACAAAGCCCTCCAGCCCCCATCGAGAAAACCATCTCCAAAGC CAAAGGGCAGCCCCGAGAACCACAGGTGTACACCTGCCCCCATCCC GGGATGAGCTGACCAAGAACCAGGTACGCTGACCTGCCTGTTCAAA GGCTTCTATCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCA GCCGGAGAACAACCTACAAGACCACGCCTCCCGTGCTGGACTCCGACG GCTCCTTCTTCTATATTCAAAGCTACCGTGGACAAGAGCAGGTGG

mAb	IgG chain	SEQ ID	Nucleic acid sequence
			CAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCA CAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCCGGAAA
	Light chain	205	GCAGCCGTGGTGACCCAGACTCCATCGTCCGTGTCTGCAGCTGTGGG AGGCACAGTCAGCATCAGTTGCCAGTCCAGTCAGAGTGTATGGTA ACAAC TACTTATCCTGGTTTCAGCAGAAACAGGGCAGCCTCCCAAG CGCCTGATGTATTCTGCATCCAGTCTGGCATCTGGGGTCCCATCGCG ATTCAGCGGCAGTGGATCTGGGACACAGTTCAC TCTCACCATCAGCG ACGTGCAGTGTGAAGATGCTGCCACTTACTACTGTCTAGGCGGTTAT GATTGTAGTTCTGATTGTAATGTTTTCGGCGGAGGGACCGAGGTGGT GGTCAAACGAACTGTGGCTGCACCATCTGTCTTCATCTTCCGCCAT CTGATGAGCAGTTGAAATCTGGAAGTGCCTCTGTTGTGTGCCTGCTG AATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTACAGAGCAGGACA GCAAGGACAGCACCTACAGCCTCAGCAGCACCTGACGCTGAGCAAA GCAGACTACGAGAAACACAAAGTCTACGCCTGCGAAGTCACCCATCA GGGCTGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGAGAGTGT
12M17	Heavy chain	221	CAGTCGTTGGAGGAGTCCGGGGGAGGCTGGTCAAGCTGAGGGATC CCTGACACTCACCTGCACAGCCTCTGGATTACCCCTCAATACTACT GGATGTGCTGGGTCCGCCAGGCTCCTGGGAAGGGGCTGGAGTGGATC GGATGCATTTATAATGGTAATGTCAGGCCATACTACGCGACCTGGGC GAAAGGCCGATTACCATCTCCAAAACCTCGTCGACCACGGTGACTC TACAAATGACCACTCTGACAGCCGCGACACGGCCACCTATTTCTGT GTGAGAGATAGTATTTTGGTGACTGGGATCCTTTTAACTTGTGGGG CCCAGGCACCTGGTCACCGTCTCCACAGCATCCACCAAGGGCCCAT CGGTCTTCCCCCTGGCACCTCTCCAAAGAGCACCTCTGGGGGCACA GCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCGAACCGGTGAC GGTGTGCTGGAACTCAGGCGCCCTGACCAGCGCGTGCACACCTTCC CGGCTGTCTACAGTCTCAGGACTCTACTCCCTCAGCAGCGTGGTG ACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGT GAATCACAAGCCCAGCAACACCAAGGTGGACAAGAAAGTTAGCCCA AATCTTGTGACAAAAC TCACATGCCACCGTGCCAGCACCTGAA CTCCTGGGGGACCGTCAGTCTTCTCTTCCCCCAAACCCAAGGA CACCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTG ACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGAC GGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGAGGAGCAGTA CAACAGCACGTACCGTGTGGTCAGCGTCTCACCCTCTGCACCAGG ACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCC CTCCCAGCCCCATCGAGAAAACCATCTCCAAGCCAAAGGGCAGCC

mAb	IgG chain	SEQ ID	Nucleic acid sequence
			CCGAGAACCACAGGTGTACACCCTGCCCCATCCCGGGATGAGCTGA CCAAGAACCAGGTGAGCTGACCTGCCTGGTCAAAGGCTTCTATCCC AGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAA CTACAAGACCACGCCCTCCCGTGTGGACTCCGACGGCTCCTTCTTCT TATATTCAAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAAC GTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACAC GCAGAAGAGCCTCTCCCTGTCTCCCGGGAAA
	Light chain	222	GCCCAAGTGCTGACCCAGACTCCAGCCTCGGTGTCTGCAGCTGTGGG AGGCACAGTCACCATCAACTGCCAGGCCAGTCAGAGTGTATATAGTA ACAACTACTTAGCCTGGTATCAGCAGAAACCAGGGCAGCCTCCCAAG CGCCTGATCTATTATGCATCCACTCTGGCATCTGGGGTCCCATCGCG GTTCAAAGGCAGTGGATCTGGGACACAGTTCCTCTCACCATCAGTG ACGTGCAGTGTGACGATGCTGCCACTTACTACTGTCAAGGCGGTTAT GATTGTAGTAGTGTGATTGTGTGCTTTCGGCGGAGGGACCGAGGT GGTGGTCAAACGAACGTGGCTGCACCATCTGTCTTCATCTTCCCGC CATCTGATGAGCAGTTGAAATCTGGAAGTGCCTCTGTGTGTGCTG CTGAATAACTTCTATCCAGAGAGGCCAAAGTACAGTGAAGTGGA TAACGCCCTCCAATCGGGTAACCTCCAGGAGAGTGTACAGAGCAGG ACAGCAAGGACAGCACCTACAGCCTCAGCAGCACCTGACGCTGAGC AAAGCAGACTACGAGAAACACAAAGTCTACGCCTGCGAAGTCACCCA TCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGAGAGT GT
12L15	Heavy chain	238	CAGGAGCAGCTGGAGGAGTCCGGGGGAGACCTGGTCAAGCCTGAGGG ATCCCTGACACTCACCTGCACAGCCTCTGGATTCTCCTTCAGTAACA GCTACTGGATATGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAG TGGATCGCATGCATTTATGCTGGTAGTAGTGGTAGCACTTACTACCC GACCTGGGCGACGGGCGGATTTCGTCTCTCCAAAACCTCGTCGACCA CGGTGACTCTGCAAATGACAGTCTGACAGCCGACACTCCGGCTTG TATTTCTGTGCGAGAGGAAGGATTATTATGATGGTCAATATGGTGC TTTTGGGTTTGCCCTACTACGGCTTGGACCTCTGGGGCCAGGGACCC TCGTCACCGTCTCTTCAGCATCCACCAAGGGCCCATCGGTCTTCCCC CTGGCACCCCTCCTCAAGAGCACCTCTGGGGGACAGCGGCCCTGGG CTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCTGTGGA ACTCAGGCGCCCTGACCAGCGCGTGCACACCTTCCCGGCTGTCTTA CAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTC CAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGC CCAGCAACACCAAGGTGGACAAGAAAGTTGAGCCCAAATCTTGTGAC AAAACTCACACATGCCACCGTGCCAGCACCTGAATCCTGGGGGG

mAb	IgG chain	SEQ ID	Nucleic acid sequence
			ACCGTCAGTCTTCCTCTTCCCCCAAACCCAGGACACCCCTCATGA TCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCAC GAAGACCCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGT GCATAATGCCAAGACAAGCCGCGGGAGGAGCAGTACAACAGCACGT ACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAAT GGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCC CATCGAGAAAACCATCTCCAAGCCAAAGGGCAGCCCCGAGAACCAC AGGTGTACACCCTGCCCCCATCCCGGATGAGCTGACCAAGAACCAG GTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGC CGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACATAAGACCA CGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTATATTCAAAG CTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATG CTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCC TCTCCCTGTCTCCCGGAAA
	Light chain	239	GCCGCCGTGCTGACCCAGACTACATCCCCCGTGTCTGCAGCTGTGGG AGGCACAGTCACCATCAATTGCCAGTCCAGTGTGAGTGTGTATAAGT ACAACTGGTTATCCTGGTATCAGCAGAAACCAGGGCAGCCTCCCAAG CTCCTGATCTATGGTGCATCCAATCTGGCGTCTGGGGTCCCATCGCG GTTCAGTGGCAGTGGATCTGGGACACAGTTCACTCTCACCATCAGCG CTGTGCAGTGTGACGATGCTGCCACTTACTACTGTGCTGGCGTTAT ATGATCGGTACTGGTCCTTTTTCGCTTTCGGCGGAGGGACCGAGGT GGTGGTGCAACGAACGTGGCTGCACCATCTGTCTTCATCTTCCCGC CATCTGATGAGCAGTTGAAATCTGGAACGCTCTGTGTGTGCTGCTG CTGAATAACTTCTATCCAGAGAGGCCAAAGTACAGTGGAAGGTGGA TAACGCCCTCCAATCGGGTAACTCCAGGAGAGTGTACAGAGCAGG ACAGCAAGGACAGCACCTACAGCCTCAGCAGCACCCGTGACGCTGAGC AAAGCAGACTACGAGAAACACAAAGTCTACGCCTGCGAAGTCACCCA TCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGAGAGT GT

[00185] In some embodiments, the sequences of the heavy chain variable domains, light chain variable domains, full-length heavy chains, and full-length light chains may be “mixed and matched” to create variants of the anti-eribulin antibodies. Such “mixed and matched” anti-eribulin antibodies can be tested using binding assays known in the art (*e.g.*, ELISAs and other assays described in the Examples). In various embodiments, the anti-eribulin antibodies disclosed herein may comprise any set of heavy and light chain variable domains listed in

Table 19 above, or the set of six CDR sequences from the heavy and light chain set. In some embodiments, the antibodies further comprise human heavy and light chain constant domains or fragments thereof. In some embodiments, the anti-eribulin antibodies may comprise a human IgG heavy chain constant domain and a human kappa light chain constant domain. In some embodiments, the anti-eribulin antibodies may comprise a human IgG1, IgG2, IgG3, or IgG4 heavy chain constant domain. In various embodiments, an anti-eribulin antibody of the present invention comprises a human immunoglobulin G subtype 1 (IgG1) heavy chain constant domain with a human Ig kappa light chain constant domain. In various embodiments, the anti-eribulin antibodies may comprise any set of full-length heavy chain and full-length light chain sequences listed in Table 20 above.

[00186] In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 17 (HCDR1), SEQ ID NO: 18 (HCDR2), and SEQ ID NO: 19 (HCDR3); and three LCDRs comprising SEQ ID NO: 20 (LCDR1), SEQ ID NO: 21 (LCDR2), and SEQ ID NO: 22 (LCDR3) as defined by the Kabat numbering system.

[00187] In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 23 (HCDR1), SEQ ID NO: 24 (HCDR2), and SEQ ID NO: 25 (HCDR3); and three LCDRs comprising SEQ ID NO: 26 (LCDR1), SEQ ID NO: 27 (LCDR2), and SEQ ID NO: 28 (LCDR3) as defined by the IMGT numbering system.

[00188] In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 89 (HCDR1), SEQ ID NO: 90 (HCDR2), and SEQ ID NO: 91 (HCDR3); and three LCDRs comprising SEQ ID NO: 92 (LCDR1), SEQ ID NO: 93 (LCDR2), and SEQ ID NO: 94 (LCDR3) as defined by the Kabat numbering system.

[00189] In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 95 (HCDR1), SEQ ID NO: 96 (HCDR2), and SEQ ID NO: 97 (HCDR3); and three LCDRs comprising SEQ ID NO: 98 (LCDR1), SEQ ID NO: 99 (LCDR2), and SEQ ID NO: 100 (LCDR3) as defined by the IMGT numbering system.

[00190] In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 107 (HCDR1),

SEQ ID NO: 108 (HCDR2), and SEQ ID NO: 109 (HCDR3); and three LCDRs comprising SEQ ID NO: 110 (LCDR1), SEQ ID NO: 111 (LCDR2), and SEQ ID NO: 112 (LCDR3) as defined by the Kabat numbering system.

[00191] In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 113 (HCDR1), SEQ ID NO: 114 (HCDR2), and SEQ ID NO: 115 (HCDR3); and three LCDRs comprising SEQ ID NO: 116 (LCDR1), SEQ ID NO: 117 (LCDR2), and SEQ ID NO: 118 (LCDR3) as defined by the IMGT numbering system.

[00192] In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 125 (HCDR1), SEQ ID NO: 126 (HCDR2), and SEQ ID NO: 127 (HCDR3); and three LCDRs comprising SEQ ID NO: 128 (LCDR1), SEQ ID NO: 129 (LCDR2), and SEQ ID NO: 130 (LCDR3) as defined by the Kabat numbering system.

[00193] In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 131 (HCDR1), SEQ ID NO: 132 (HCDR2), and SEQ ID NO: 133 (HCDR3); and three LCDRs comprising SEQ ID NO: 134 (LCDR1), SEQ ID NO: 135 (LCDR2), and SEQ ID NO: 136 (LCDR3) as defined by the IMGT numbering system.

[00194] In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 143 (HCDR1), SEQ ID NO: 144 (HCDR2), and SEQ ID NO: 145 (HCDR3); and three LCDRs comprising SEQ ID NO: 146 (LCDR1), SEQ ID NO: 129 (LCDR2), and SEQ ID NO: 147 (LCDR3) as defined by the Kabat numbering system.

[00195] In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 148 (HCDR1), SEQ ID NO: 149 (HCDR2), and SEQ ID NO: 150 (HCDR3); and three LCDRs comprising SEQ ID NO: 151 (LCDR1), SEQ ID NO: 135 (LCDR2), and SEQ ID NO: 152 (LCDR3) as defined by the IMGT numbering system.

[00196] In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 159 (HCDR1), SEQ ID NO: 160 (HCDR2), and SEQ ID NO: 161 (HCDR3); and three LCDRs comprising

SEQ ID NO: 162 (LCDR1), SEQ ID NO: 21 (LCDR2), and SEQ ID NO: 163 (LCDR3) as defined by the Kabat numbering system.

[00197] In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 164 (HCDR1), SEQ ID NO: 165 (HCDR2), and SEQ ID NO: 166 (HCDR3); and three LCDRs comprising SEQ ID NO: 167 (LCDR1), SEQ ID NO: 27 (LCDR2), and SEQ ID NO: 168 (LCDR3) as defined by the IMGT numbering system.

[00198] In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 175 (HCDR1), SEQ ID NO: 176 (HCDR2), and SEQ ID NO: 109 (HCDR3); and three LCDRs comprising SEQ ID NO: 177 (LCDR1), SEQ ID NO: 111 (LCDR2), and SEQ ID NO: 178 (LCDR3) as defined by the Kabat numbering system.

[00199] In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 179 (HCDR1), SEQ ID NO: 180 (HCDR2), and SEQ ID NO: 115 (HCDR3); and three LCDRs comprising SEQ ID NO: 181 (LCDR1), SEQ ID NO: 117 (LCDR2), and SEQ ID NO: 182 (LCDR3) as defined by the IMGT numbering system.

[00200] In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 189 (HCDR1), SEQ ID NO: 190 (HCDR2), and SEQ ID NO: 191 (HCDR3); and three LCDRs comprising SEQ ID NO: 192 (LCDR1), SEQ ID NO: 193 (LCDR2), and SEQ ID NO: 194 (LCDR3) as defined by the Kabat numbering system.

[00201] In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 195 (HCDR1), SEQ ID NO: 196 (HCDR2), and SEQ ID NO: 197 (HCDR3); and three LCDRs comprising SEQ ID NO: 198 (LCDR1), SEQ ID NO: 117 (LCDR2), and SEQ ID NO: 199 (LCDR3) as defined by the IMGT numbering system.

[00202] In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 206 (HCDR1), SEQ ID NO: 207 (HCDR2), and SEQ ID NO: 208 (HCDR3); and three LCDRs comprising SEQ ID NO: 44 (LCDR1), SEQ ID NO: 209 (LCDR2), and SEQ ID NO: 210 (LCDR3) as defined by the Kabat numbering system.

[00203] In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 211 (HCDR1), SEQ ID NO: 212 (HCDR2), and SEQ ID NO: 213 (HCDR3); and three LCDRs comprising SEQ ID NO: 214 (LCDR1), SEQ ID NO: 215 (LCDR2), and SEQ ID NO: 216 (LCDR3) as defined by the IMGT numbering system.

[00204] In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 223 (HCDR1), SEQ ID NO: 224 (HCDR2), and SEQ ID NO: 225 (HCDR3); and three LCDRs comprising SEQ ID NO: 226 (LCDR1), SEQ ID NO: 227 (LCDR2), and SEQ ID NO: 228 (LCDR3) as defined by the Kabat numbering system.

[00205] In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 229 (HCDR1), SEQ ID NO: 230 (HCDR2), and SEQ ID NO: 231 (HCDR3); and three LCDRs comprising SEQ ID NO: 232 (LCDR1), SEQ ID NO: 99 (LCDR2), and SEQ ID NO: 233 (LCDR3) as defined by the IMGT numbering system.

[00206] In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 29, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 30. In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 101, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 102. In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 119, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 120. In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 137, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 138. In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 153, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 154. In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 169, and a light chain

variable region comprising the amino acid sequence of SEQ ID NO: 170. In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 183, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 184. In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 200, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 201. In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 217, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 218. In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 234, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 235.

[00207] In some embodiments, an anti-eribulin antibody or antigen-binding fragment comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 29, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 30.

[00208] In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises three HCDRs from the heavy chain variable region comprising SEQ ID NO: 29, and three LCDRs from the light chain variable region comprising SEQ ID NO: 30. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises three HCDRs from the heavy chain variable region comprising SEQ ID NO: 101, and three LCDRs from the light chain variable region comprising SEQ ID NO: 102. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises three HCDRs from the heavy chain variable region comprising SEQ ID NO: 119, and three LCDRs from the light chain variable region comprising SEQ ID NO: 120. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises three HCDRs from the heavy chain variable region comprising SEQ ID NO: 137, and three LCDRs from the light chain variable region comprising SEQ ID NO: 138. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises three HCDRs from the heavy chain variable region comprising SEQ ID NO: 153, and three LCDRs from the light chain variable region comprising SEQ ID NO: 154. In some embodiments, an

anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises three HCDRs from the heavy chain variable region comprising SEQ ID NO: 169, and three LCDRs from the light chain variable region comprising SEQ ID NO: 170. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises three HCDRs from the heavy chain variable region comprising SEQ ID NO: 183, and three LCDRs from the light chain variable region comprising SEQ ID NO: 184. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises three HCDRs from the heavy chain variable region comprising SEQ ID NO: 200, and three LCDRs from the light chain variable region comprising SEQ ID NO: 201. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises three HCDRs from the heavy chain variable region comprising SEQ ID NO: 217, and three LCDRs from the light chain variable region comprising SEQ ID NO: 218. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises three HCDRs from the heavy chain variable region comprising SEQ ID NO: 234, and three LCDRs from the light chain variable region comprising SEQ ID NO: 235.

[00209] In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises three HCDRs from the heavy chain variable region comprising SEQ ID NO: 29, and three LCDRs from the light chain variable region comprising SEQ ID NO: 30.

[00210] In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a heavy chain variable region with at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 29. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a heavy chain variable region with at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 101. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a heavy chain variable region with at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 119. In some embodiments, an anti-eribulin

antibody or antigen-binding fragment thereof provided herein comprises a heavy chain variable region with at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 153. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a heavy chain variable region with at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 169. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a heavy chain variable region with at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 183. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a heavy chain variable region with at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 200. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a heavy chain variable region with at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 217. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a heavy chain variable region with at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 234.

[00211] In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a light chain variable region with at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 30. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a light chain variable region with at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least

92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 102. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a light chain variable region with at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 120. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a light chain variable region with at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 154. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a light chain variable region with at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 170. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a light chain variable region with at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 184. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a light chain variable region with at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 201. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a light chain variable region with at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 218. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a light chain variable region with at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 235.

[00212] In various embodiments, the anti-eribulin antibody or antigen-binding fragment is an antigen-binding fragment. In some embodiments, an anti-eribulin antigen-binding fragment is a Fab fragment.

[00213] In some embodiments, an anti-eribulin antibody or antigen-binding fragment provided herein comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 31. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a light chain comprising an amino acid sequence of SEQ ID NO: 32. In some embodiments, the anti-eribulin antibody or antigen-binding fragment is a Fab fragment.

[00214] In various embodiments, the anti-eribulin antibodies comprise a human IgG heavy chain constant domain. In some embodiments, the IgG heavy chain constant domain is IgG1.

[00215] In various embodiments, the anti-eribulin antibodies comprise a human Ig kappa light chain constant region. In various embodiments, the anti-eribulin antibodies comprise a human Ig lambda light chain constant region.

[00216] In some embodiments, an anti-eribulin antibody or antigen-binding fragment provided herein comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 294. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a light chain comprising an amino acid sequence of SEQ ID NO: 32. In some embodiments, an anti-eribulin antibody or antigen-binding fragment provided herein comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 103. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a light chain comprising an amino acid sequence of SEQ ID NO: 104. In some embodiments, an anti-eribulin antibody or antigen-binding fragment provided herein comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 121. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a light chain comprising an amino acid sequence of SEQ ID NO: 122. In some embodiments, an anti-eribulin antibody or antigen-binding fragment provided herein comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 139. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a light chain comprising an amino acid sequence of SEQ ID NO: 140. In some embodiments, an anti-eribulin antibody or antigen-binding fragment provided herein comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 155. In some

embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a light chain comprising an amino acid sequence of SEQ ID NO: 156. In some embodiments, an anti-eribulin antibody or antigen-binding fragment provided herein comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 171. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a light chain comprising an amino acid sequence of SEQ ID NO: 172. In some embodiments, an anti-eribulin antibody or antigen-binding fragment provided herein comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 185. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a light chain comprising an amino acid sequence of SEQ ID NO: 186. In some embodiments, an anti-eribulin antibody or antigen-binding fragment provided herein comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 202. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a light chain comprising an amino acid sequence of SEQ ID NO: 203. In some embodiments, an anti-eribulin antibody or antigen-binding fragment provided herein comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 219. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a light chain comprising an amino acid sequence of SEQ ID NO: 220. In some embodiments, an anti-eribulin antibody or antigen-binding fragment provided herein comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 236. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a light chain comprising an amino acid sequence of SEQ ID NO: 237.

[00217] In some embodiments, an anti-eribulin antibody or antigen-binding fragment provided herein comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 294. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a light chain comprising an amino acid sequence of SEQ ID NO: 32. In some embodiments, the anti-eribulin antibody or antigen-binding fragment comprises a human IgG1 heavy chain constant domain.

[00218] In some embodiments, an anti-eribulin antibody or antigen-binding fragment provided herein is antibody 5E4. In some embodiments, 5E4 is a Fab. In some embodiments, an anti-eribulin antibody or antigen-binding fragment provided herein is antibody 5P14.

[00219] In some embodiments, an anti-eribulin antibody or antigen-binding fragment provided herein is conjugated to a label. In some embodiments, the anti-eribulin antibody or antigen-binding fragment is conjugated to a fluorescent tag. In some embodiments, the anti-eribulin antibody or antigen-binding fragment is conjugated to a biotin moiety. In some embodiments, the anti-eribulin antibody or antigen-binding fragment is conjugated to a streptavidin. In some embodiments, the anti-eribulin antibody or antigen-binding fragment is conjugated to an enzyme reporter. In some embodiments, the anti-eribulin antibody or antigen-binding fragment is conjugated to a bead. In some embodiments, the bead is an agarose bead or a magnetic bead.

[00220] In some embodiments, an anti-eribulin antibody or antigen-binding fragment provided herein is conjugated to an agarose bead or a magnetic bead.

[00221] In some embodiments, an anti-eribulin antibody or antigen-binding fragment provided herein is conjugated to a biotin. In some embodiments, the anti-eribulin antibody or antigen-binding fragment is immobilized on a solid surface.

[00222] In some embodiments, an anti-eribulin antibody or antigen-binding fragment provided herein binds to eribulin with a binding affinity of at least 0.1 nM, at least 0.2 nM, at least 0.3 nM, at least 0.4 nM, at least 0.5 nM, at least 0.6 nM, at least 0.7 nM, at least 0.8 nM, at least 0.9 nM, at least 1.0 nM, at least 1.1 nM, at least 1.2 nM, at least 1.3 nM, at least 1.4 nM, at least 1.5 nM, at least 2.0 nM, at least 2.5 nM, at least 3.0 nM, at least 3.5 nM, at least 4.0 nM, at least 4.5 nM, at least 5.0 nM, at least 5.5 nM, at least 6.0 nM, at least 6.5 nM, at least 7.0 nM, at least 7.5 nM, at least 8.0 nM, at least 8.5 nM, at least 9.0 nM, at least 9.5 nM, or at least 10.0 nM.

Linkers and Linker-Payload Conjugates

[00223] In various embodiments, an antibody or antigen-binding fragment disclosed herein specifically binds to a linker or linker-payload conjugate. An exemplary linker or linker-payload conjugate comprises VCP.

[00224] In some embodiments, the linker in an ADC is stable extracellularly in a sufficient manner to be therapeutically effective. In some embodiments, the linker is stable outside a cell, such that the ADC remains primarily intact when present in extracellular conditions (e.g., prior to transport or delivery into a cell). As used herein, “stable,” in the context of a linker or ADC comprising a linker, means that no more than 20%, no more than about 15%,

no more than about 10%, no more than about 5%, no more than about 3%, or no more than about 1% of the linkers (or any percentage in between) in a sample of ADC are cleaved (or in the case of an overall ADC are otherwise not intact) when the ADC is present in extracellular conditions. In some embodiments, the ADC is metabolized in circulation such that a linker-payload is cleaved from the ADC.

[00225] Whether a linker is stable extracellularly can be determined, for example, by including an ADC in plasma for a predetermined time period (e.g., 2, 4, 6, 8, 16, or 24 hours) and then quantifying the amount of free linker-payload and/or free drug moiety present in the plasma. Stability may allow the ADC time to localize to target tumor cells and prevent the premature release of the drug, which could lower the therapeutic index of the ADC by indiscriminately damaging both normal and tumor tissues. In some embodiments, the linker is stable outside of a target cell and releases the drug moiety from the ADC once inside of the cell, such that the drug moiety can bind to its target (e.g., to microtubules). Thus, an effective linker will: (i) maintain the specific binding properties of the antibody moiety; (ii) allow delivery, e.g., intracellular delivery, of the drug moiety via stable attachment to the antibody moiety; (iii) remain stable and intact until the ADC has been transported or delivered to its target site; and (iv) allow for the therapeutic effect, e.g., cytotoxic effect, of the drug moiety after cleavage. In determining the efficacy of a linker, it is beneficial to be able to measure linker or linker-payload metabolites.

[00226] A linker may be “cleavable” or “non-cleavable” (Ducry and Stump, *Bioconjugate Chem.* (2010) 21:5-13). Cleavable linkers are designed to release the drug when subjected to certain environment factors, e.g., when internalized into a target cell, whereas non-cleavable linkers generally rely on the degradation of the antibody moiety itself.

[00227] In some embodiments, the linker is a cleavable linker. A cleavable linker refers to any linker that comprises a cleavable moiety. As used herein, the term “cleavable moiety” refers to any chemical bond that can be cleaved. Suitable cleavable chemical bonds are known in the art and include, but are not limited to, acid labile bonds, protease/peptidase labile bonds, photolabile bonds, disulfide bonds, and esterase labile bonds. Linkers comprising a cleavable moiety can allow for the release of the drug moiety from the ADC via cleavage at a particular site in the linker. In various embodiments, cleavage of the antibody from the linked payload activates or increases the activity of the payload. Exemplary

cleavable linkers include acid labile linkers, protease/peptidase-sensitive linkers, photolabile linkers, dimethyl-, disulfide-, or sulfonamide-containing linkers.

[00228] In some embodiments, the linker is cleavable by a cleaving agent, e.g., an enzyme, that is present in the intracellular environment (e.g., within a lysosome or endosome or caveola). The linker can be, e.g., a peptide linker that is cleaved by an intracellular peptidase or protease enzyme, including, but not limited to, a lysosomal or endosomal protease. In some embodiments, the linker is a cleavable peptide linker. As used herein, a cleavable peptide linker refers to any linker that comprises a cleavable peptide moiety. The term “cleavable peptide moiety” refers to any chemical bond linking amino acids (natural or synthetic amino acid derivatives) that can be cleaved by an agent that is present in the intracellular environment. For instance, a linker may comprise an alanine-alanine-asparagine (Ala-Ala-Asn) sequence, a valine-alanine (Val-Ala) sequence, or a valine-citrulline (Val-Cit) sequence that is cleavable by a peptidase such as cathepsin, e.g., cathepsin B.

[00229] In some embodiments, the linker in any of the ADCs disclosed herein may comprise at least one spacer unit joining the antibody moiety to the drug moiety. In some embodiments, the spacer unit joins a cleavage site (e.g., a cleavable peptide moiety) in the linker to the antibody moiety. In some embodiments, the linker, and/or spacer unit in the linker, is substantially hydrophilic. A hydrophilic linker may be used to reduce the extent to which the drug may be pumped out of resistant cancer cells through multiple drug resistance (MDR) or functionally similar transporters. In some aspects, the linker includes one or more polyethylene glycol (PEG) moieties, e.g., 1, 2, 3, 4, 5, or 6 PEG moieties.

[00230] In some embodiments, the spacer unit in the linker comprises one or more PEG moieties. In some embodiments, the spacer unit comprises $-(\text{PEG})_m-$, and m is an integer from 1 to 10. In some embodiments, m ranges from 1 to 10; from 2 to 8; from 2 to 6; from 2 to 5; from 2 to 4; or from 2 to 3. In some embodiments, m is 8. In some embodiments, m is 4. In some embodiments, m is 3. In some embodiments, m is 2. In some embodiments, the spacer unit comprises $(\text{PEG})_2$, $(\text{PEG})_4$, $(\text{PEG})_8$, $(\text{PEG})_9$, $(\text{PEG})_3$ -triazole- $(\text{PEG})_3$, $(\text{PEG})_4$ -triazole- $(\text{PEG})_3$, or dibenzylcyclooctene-triazole- $(\text{PEG})_3$. In some preferred embodiments, the spacer unit comprises $(\text{PEG})_2$.

[00231] In some embodiments, the spacer unit in the linker comprises an alkyl moiety. In some embodiments, the spacer unit comprises $-(\text{CH}_2)_n-$, and n is an integer from 1 to 10 (i.e., n may be 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10). In some embodiments, n is 5.

[00232] A spacer unit may be used, for example, to link the antibody moiety to the drug moiety, either directly or indirectly. In some embodiments, the spacer unit links the antibody moiety to the drug moiety directly. In some embodiments, the antibody moiety and the drug moiety are attached via a spacer unit comprising one or more PEG moieties (e.g., (PEG)₂ or (PEG)₄). In some embodiments, the spacer unit links the antibody moiety to the drug moiety indirectly. In some embodiments, the spacer unit links the antibody moiety to the drug moiety indirectly through a cleavable moiety (e.g., a cleavable peptide, a cleavable disulfide, or a cleavable sulfonamide) and/or an attachment moiety to join the spacer unit to the antibody moiety, e.g., a maleimide moiety.

[00233] The spacer unit, in various embodiments, attaches to the antibody moiety (i.e., the antibody or antigen-binding fragment) via a maleimide moiety (Mal). The term “maleimide moiety,” as used herein, means a compound that contains a maleimide group and that is reactive with a sulfhydryl group, e.g., a sulfhydryl group of a cysteine residue on the antibody moiety. Other functional groups that are reactive with sulfhydryl groups (thiols) include, but are not limited to, iodoacetamide, bromoacetamide, vinyl pyridine, disulfide, pyridyl disulfide, isocyanate, and isothiocyanate. In some embodiments, the Mal is reactive with a cysteine residue on the antibody or antigen-binding fragment. In some embodiments, the Mal is joined to the antibody or antigen-binding fragment via the cysteine residue.

[00234] In certain embodiments, the linker comprises a Mal moiety, a spacer unit, and a cleavable peptide moiety. In some embodiments, the cleavable peptide moiety comprises an amino acid unit. In some embodiments, the amino acid unit comprises Val-Cit. In some embodiments, the linker comprises the Mal, a spacer unit, and Val-Cit. In some embodiments, the linker comprises Mal-(PEG)₂-Val-Cit. In some embodiments, the linker comprises Mal-(PEG)_{*m*}-Val-Cit, where *m* is 2 to 8 or 2 to 5, or 2, 3, 4, or 5. In some embodiments, the linker comprises Mal-(PEG)₈-Val-Cit. In some embodiments, the Mal-spacer unit comprises a maleimidocaproyl (MC). In some embodiments, the linker comprises MC-Val-Cit.

[00235] In some embodiments, the linker comprises the Mal, a spacer unit, and Val-Ala. In some embodiments, the linker comprises Mal-(PEG)₂-Val-Ala. In some embodiments, the linker comprises Mal-(PEG)_{*m*}-Val-Ala, where *m* is 2 to 8 or 2 to 5, or 2, 3, 4, or 5. In some embodiments, the linker comprises Mal-(PEG)₈-Val-Ala. In some embodiments, the Mal-

spacer unit comprises a maleimidocaproyl (MC). In some embodiments, the linker comprises MC-Val-Ala.

[00236] In various embodiments, the spacer unit attaches to the antibody or antigen-binding fragment via a succinimide moiety (OSu). The term “succinimide moiety,” as used herein, means a compound that contains a succinimide compound that is reactive with an amine group, e.g., an amine group of a lysine residue on the antibody moiety. An exemplary succinimide moiety is N-hydroxysuccinimide (NHS). In some embodiments, the OSu-spacer unit is reactive with a lysine residue on the antibody or antigen-binding fragment. In some embodiments, the OSu-spacer unit is joined to the antibody or antigen-binding fragment via the lysine residue.

[00237] In certain embodiments, the linker comprises an OSu, a spacer unit, and a cleavable peptide moiety. In some embodiments, the cleavable peptide moiety comprises an amino acid unit. In some embodiments, the amino acid unit comprises Val-Cit. In some embodiments, the linker comprises an OSu, a spacer unit, and Val-Cit. In some embodiments, the linker comprises OSu-(PEG)₂-Val-Cit. In other embodiments, the linker comprises OSu-(PEG)₉-Val-Cit. In other embodiments, the linker comprises OSu-(CH₂)₅-Val-Cit. In certain embodiments, the linker comprises OSu-(PEG)₃-triazole-(PEG)₃-Val-Cit.

[00238] In various embodiments, the cleavable moiety in the linker is joined directly to the payload moiety. In other embodiments, another spacer unit is used to attach the cleavable moiety in the linker to the payload moiety. In various embodiments, the payload moiety is eribulin. In various embodiments, the eribulin is attached to the cleavable moiety in the linker by a spacer unit. In some embodiments, the eribulin is attached to the cleavable moiety in the linker by a self-immolative spacer unit. In certain embodiments, the eribulin is attached to the cleavable moiety in the linker by a self-immolative spacer unit, the cleavable moiety comprises Val-Cit, and a further spacer unit comprising PEG joins the cleavable moiety to the antibody moiety. In certain embodiments, the eribulin is joined to an anti-FRA antibody via a Mal-spacer unit in the linker joined to a Val-Cit cleavable moiety and a pAB self-immolative spacer unit. In certain other embodiments, the eribulin is joined to an anti-MSLN antibody via a Mal-spacer unit in the linker joined to a Val-Cit cleavable moiety and a pAB self-immolative spacer unit.

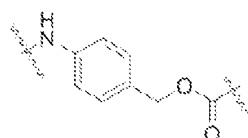
[00239] A spacer unit may be “self-immolative” or “non-self-immolative.” A “non-self-immolative” spacer unit is one in which part or all of the spacer unit remains bound to the

drug moiety upon cleavage of the linker. Examples of non-self-immolative spacer units include, but are not limited to, a glycine spacer unit and a glycine-glycine spacer unit. Non-self-immolative spacer units may eventually degrade over time but do not readily release a linked native drug entirely under cellular conditions. A “self-immolative” spacer unit allows for release of the native drug moiety under intracellular conditions. A “native drug” is one where no part of the spacer unit or other chemical modification remains after cleavage/degradation of the spacer unit.

[00240] Self-immolation chemistry is known in the art and could be readily selected for the disclosed linkers and/or ADCs. In various embodiments, the spacer unit attaching the cleavable moiety in the linker to the drug moiety (e.g., eribulin) is self-immolative, and undergoes self-immolation concurrently with or shortly before/after cleavage of the cleavable moiety under intracellular conditions.

[00241] In certain embodiments, the self-immolative spacer unit in the linker comprises a p-aminobenzyl unit. In some embodiments, a p-aminobenzyl alcohol (pABOH) is attached to an amino acid unit or other cleavable moiety in the linker via an amide bond, and a carbamate, methylcarbamate, or carbonate is made between the pABOH and the drug moiety (Hamann et al. (2005) Expert Opin. Ther. Patents 15:1087-103). In some embodiments, the self-immolative spacer unit is or comprises p-aminobenzylloxycarbonyl (pAB). Without being bound by theory, it is thought that the self-immolation of pAB involves a spontaneous 1,6-elimination reaction (Jain et al. (2015) Pharm Res 32:3526-40).

[00242] In various embodiments, the structure of the p-aminobenzylloxycarbonyl (pAB) used in the disclosed ADCs is shown below:



p-amino-benzyloxycarbonyl

[00243] In various embodiments, the self-immolative spacer unit attaches the cleavable moiety in the linker to the C-35 amine on eribulin. In some embodiments, the self-immolative spacer unit is pAB. In some embodiments, the pAB attaches the cleavable moiety in the linker to the C-35 amine on eribulin. In some embodiments, the pAB undergoes self-immolation upon cleavage of the cleavable moiety, and eribulin is released from the ADC in

its native, active form. In some embodiments, an anti-FRA antibody (e.g., MORAb-003) is joined to the C-35 amine of eribulin by a linker comprising Mal-(PEG)₂-Val-Cit-pAB. In other embodiments, an anti-MSLN antibody (e.g., 345A12) is joined to the C-35 amine of eribulin by a linker comprising Mal-(PEG)₂-Val-Cit-pAB. In some embodiments, an anti-FRA antibody (e.g., MORAb-003) is joined to the C-35 amine of eribulin by a linker comprising MC-Val-Cit-pAB. In other embodiments, an anti-MSLN antibody (e.g., 345A12) is joined to the C-35 amine of eribulin by a linker comprising MC-Val-Cit-pAB. In other embodiments, an anti-HER2 antibody (e.g., trastuzumab) is joined to the C-35 amine of eribulin by a linker comprising MC-Val-Cit-pAB.

[00244] In some embodiments, an anti-FRA antibody (e.g., MORAb-003) is joined to the C-35 amine of eribulin by a linker comprising Mal-(PEG)₂-Val-Ala-pAB. In other embodiments, an anti-MSLN antibody (e.g., 345A12) is joined to the C-35 amine of eribulin by a linker comprising Mal-(PEG)₂-Val-Ala-pAB. In other embodiments, an anti-HER2 antibody (e.g., trastuzumab) is joined to the C-35 amine of eribulin by a linker comprising Mal-(PEG)₂-Val-Ala-pAB. In some embodiments, an anti-FRA antibody (e.g., MORAb-003) is joined to the C-35 amine of eribulin by a linker comprising MC-Val-Ala-pAB. In other embodiments, an anti-MSLN antibody (e.g., 345A12) is joined to the C-35 amine of eribulin by a linker comprising MC-Val-Ala-pAB. In other embodiments, an anti-HER2 antibody (e.g., trastuzumab) is joined to the C-35 amine of eribulin by a linker comprising MC-Val-Ala-pAB.

[00245] In various aspects, the antibody moiety of the ADC is conjugated to the drug moiety via a linker, wherein the linker comprises a Mal-spacer unit, a cleavable amino acid unit, and a pAB. In some embodiments, the spacer unit comprises a PEG moiety. In some embodiments, the spacer unit comprises an alkyl moiety. In some embodiments, the linker comprises Mal-(PEG)₂-Val-Cit-pAB. In some embodiments, the linker comprises Mal-(PEG)₈-Val-Cit-pAB. In some embodiments, the linker comprises Mal-(CH₂)₅-Val-Cit-pAB.

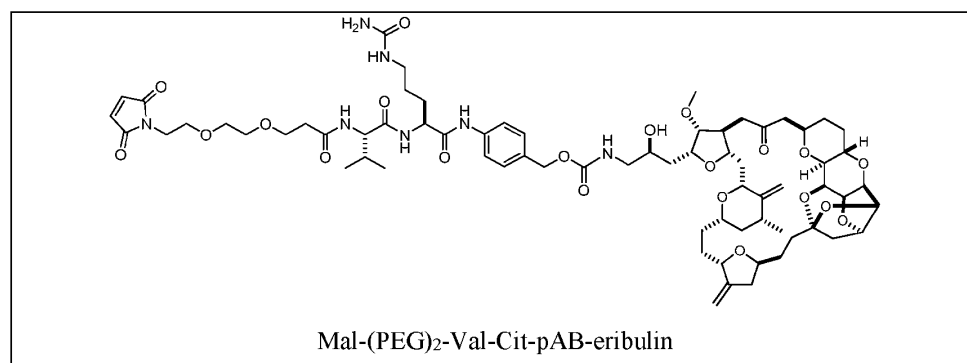
[00246] In some aspects, the antibody moiety of the ADC is conjugated to the drug moiety via a linker, wherein the linker comprises OSu-spacer unit-amino acid unit-pAB. In some embodiments, the spacer unit comprises a PEG moiety. In some embodiments, the spacer unit comprises an alkyl moiety. In some embodiments, the linker comprises OSu-(PEG)₂-amino acid unit-pAB. In some embodiments, the linker comprises OSu-(PEG)₂-Val-Cit-pAB. In some embodiments, the linker comprises OSu-(PEG)₉-Val-Cit-pAB. In some embodiments,

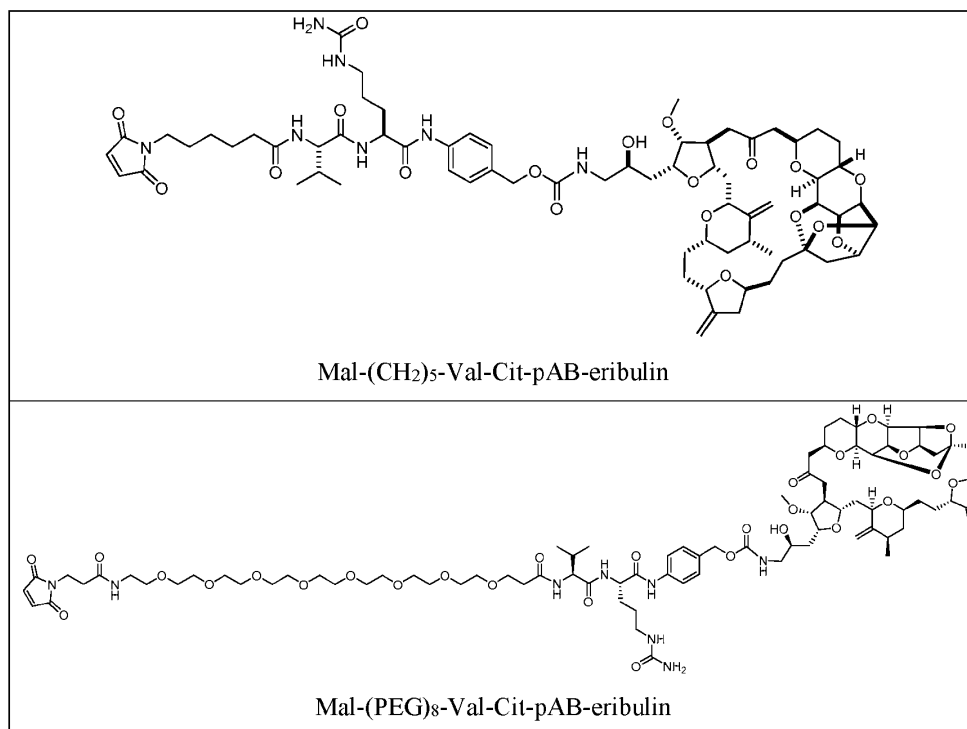
the linker comprises OSu-(CH₂)₅-Val-Cit-pAB. In some embodiments, the linker comprises OSu-(PEG)₃-triazole-(PEG)₃-Val-Cit-pAB.

[00247] In some embodiments, an anti-VCP antibody disclosed herein specifically binds a linker comprising VCP. In some embodiments, an anti-VCP antibody disclosed herein specifically binds a linker conjugate comprising Mal-(PEG)_m-VCP. In some embodiments, an anti-VCP antibody disclosed herein specifically binds a linker conjugate comprising Mal-(PEG)₂-VCP. In some embodiments, an anti-VCP antibody disclosed herein specifically binds a linker-payload conjugate comprising VCP. In some embodiments, an anti-VCP antibody disclosed herein specifically binds a linker-payload conjugate comprising VCP-eribulin. In some embodiments, an anti-VCP antibody disclosed herein specifically binds a linker-payload conjugate comprising Mal-(PEG)_m-VCP-eribulin. In some embodiments, an anti-VCP antibody disclosed herein specifically binds a linker-payload conjugate comprising Mal-(PEG)₂-VCP-eribulin.

[00248] Exemplary linkers and linker-payload conjugates are shown below in Table 22.

Table 22. Exemplary Linker-Payload Compounds





[00249] In various embodiments, anti-linker antibodies or antigen-binding fragments may be designed as taught herein to specifically bind linkers or linker-payload conjugates comprising an alternative (e.g., non-VCP) cleavable or non-cleavable linker moiety. Alternative linker moieties are known in the art. Exemplary cleavable linker moieties include, for example, a disulfide moiety, a sulfonamide moiety, or an amino acid unit. Exemplary amino acid units include, but are not limited to, dipeptides, tripeptides, tetrapeptides, and pentapeptides. Exemplary dipeptides include, but are not limited to, valine-citrulline (Val-Cit), alanine-asparagine (Ala-Asn), alanine-phenylalanine (Ala-Phe), phenylalanine-lysine (Phe-Lys), alanine-lysine (Ala-Lys), alanine-valine (Ala-Val), valine-alanine (Val-Ala), valine-lysine (Val-Lys), lysine-lysine (Lys-Lys), phenylalanine-citrulline (Phe-Cit), leucine-citrulline (Leu-Cit), isoleucine-citrulline (Ile-Cit), tryptophan-citrulline (Trp-Cit), and phenylalanine-alanine (Phe-Ala). Exemplary tripeptides include, but are not limited to, alanine-alanine-asparagine (Ala-Ala-Asn), glycine-valine-citrulline (Gly-Val-Cit), glycine-glycine-glycine (Gly-Gly-Gly), phenylalanine-phenylalanine-lysine (Phe-Phe-Lys), and glycine-phenylalanine-lysine (Gly-Phe-Lys). Other exemplary amino acid units include, but

are not limited to, Gly-Phe-Leu-Gly, Ala-Leu-Ala-Leu, Phe-N⁹-tosyl-Arg, and Phe-N⁹-Nitro-Arg, as described in, e.g., U.S. Pat. No. 6,214,345. In some embodiments, the linker or linker-payload comprises a cleavable amino acid unit and eribulin.

Anti-VCP Antibodies and Antigen-Binding Fragments

[00250] The present disclosure also provides antibodies or antigen-binding fragments thereof that specifically bind a linker or a linker-payload conjugate comprising VCP, e.g., which may be used in any of the assays disclosed herein. An anti-VCP antibody may bind the linker by binding an epitope on the linker. Alternatively, an anti-VCP antibody may bind an epitope formed from the linker-payload but not present in the linker alone.

[00251] The antibodies or antigen binding fragments disclosed herein that specifically bind VCP may comprise three HC CDRs (HCDR1, HCDR2, and HCDR3) having amino acid sequences selected from the HC CDRs listed in Table 23, *infra*, as defined by the Kabat numbering system, and three light chain CDRs (LCDR1, LCDR2, and LCDR3) having amino acid sequences selected from the LC CDRs listed in Table 23, *infra*, as defined by the Kabat numbering system. In some embodiments, the anti-VCP antibodies comprise three heavy chain CDRs (HCDR1, HCDR2, and HCDR3) having amino acid sequences selected from the HC CDRs listed in Table 24, *infra*, as defined by the IMGT numbering system, and three light chain CDRs (LCDR1, LCDR2, and LCDR3) having amino acid sequences selected from the LC CDRs listed in Table 24, *infra*, as defined by the IMGT numbering system.

[00252] In some embodiments, an anti-VCP antibody disclosed herein comprises a VH domain having an amino acid sequence selected from SEQ ID NOs: 45 and 248 listed in Table 25, *infra*. In some embodiments, the antibody comprises a VL domain having an amino acid sequence selected from SEQ ID NOs: 46 and 249 listed in Table 25, *infra*.

[00253] In some embodiments, an antigen-binding fragment disclosed herein is a variant that retains VCP binding. In some embodiments, the antigen-binding fragment retains VCP binding by comprising three heavy chain CDRs (HCDR1, HCDR2, and HCDR3) comprising amino acid sequences selected from the HC CDRs listed in Table 23, *infra*, as defined by the Kabat numbering system, and three light chain CDRs (LCDR1, LCDR2, and LCDR3) comprising amino acid sequences selected from the LC CDRs listed in Table 23, *infra*, as defined by the Kabat numbering system. In some embodiments, the antigen-binding fragment comprises three heavy chain CDRs (HCDR1, HCDR2, and HCDR3) comprising amino acid

sequences selected from the HC CDRs listed in Table 24, *infra*, as defined by the IMGT numbering system, and three light chain CDRs (LCDR1, LCDR2, and LCDR3) comprising amino acid sequences selected from the LC CDRs listed in Table 24, *infra*, as defined by the IMGT numbering system. In some embodiments, the antigen-binding fragments disclosed herein may retain VCP binding by comprising a VH domain comprising an amino acid sequence selected from SEQ ID NOs: 45 and 248 listed in Table 25, *infra*, and a VL domain comprising an amino acid sequence selected from SEQ ID NOs: 46 and 249 listed in Table 25, *infra*.

[00254] In some embodiments, an anti-VCP antibody or antigen-binding fragment further comprises human heavy and light chain frameworks (optionally with one or more backmutations to improve binding affinity) and/or human heavy and light chain constant domains or fragments thereof. For instance, the antibody or antigen-binding fragment may comprise a human IgG heavy chain constant domain (such as an IgG1) and a human kappa or lambda light chain constant domain. In some embodiments, the antibody or antigen-binding fragment comprises a human IgG1 heavy chain constant domain with a human Ig kappa light chain constant domain.

[00255] In some embodiments, an antibody that specifically binds VCP comprises a heavy chain having an amino acid sequence selected from SEQ ID NOs: 47 and 250 listed in Table 26, *infra*. In some embodiments, an antibody that specifically binds VCP comprises a light chain having an amino acid sequence selected from SEQ ID NOs: 48 and 251 listed in Table 26, *infra*.

[00256] Amino acid and nucleic acid sequences of exemplary anti-VCP antibodies of the present disclosure are set forth in Tables 23-27.

Table 23. Amino acid sequences of Kabat CDRs for anti-VCP antibodies

mAb	IgG chain	SEQ ID	Amino acid sequence
11G6	HC CDR1	33	YYGVS
	HC CDR2	34	CIFPGFGITNYANSVKGR
	HC CDR3	35	EYGSPSGYYGVGYHSP L
	LC CDR1	36	QSSQSVYKNNWLS
	LC CDR2	37	AASNLES
	LC CDR3	38	AGGYSSSSDYA

mAb	IgG chain	SEQ ID	Amino acid sequence
6O11	HC CDR1	159	SSYWIC
	HC CDR2	240	CINSGSGFTYYASWVNG
	HC CDR3	241	AGNDGWGEDL
	LC CDR1	242	QASQSIVSYCS
	LC CDR2	209	YASTLAS
	LC CDR3	243	QNNNGVNGRGTP

Table 24. Amino acid sequences of IMGT CDRs for anti-VCP antibodies

mAb	IgG chain	SEQ ID	Amino acid sequence
11G6	HC CDR1	39	GIDLSYYG
	HC CDR2	40	IFPGFGITN
	HC CDR3	41	AREYGSPSGYYGVGYHSPL
	LC CDR1	42	QSVYKNNW
	LC CDR2	43	AAS
	LC CDR3	38	AGGYSSSSDYA
6O11	HC CDR1	164	GFSFSSSYW
	HC CDR2	244	INSGSGFT
	HC CDR3	245	ARAGNDGWGEDL
	LC CDR1	246	QSIVSY
	LC CDR2	219	YAS
	LC CDR3	243	QNNNGVNGRGTP

Table 25. Amino acid sequences of variable regions for anti-VCP antibodies

mAb	IgG chain	SEQ ID	Amino acid sequence
11G6	VH	45	QEQLVESGGGLVQPGESLKLCKVSGIDLSYYGVSWV RQAPGKGPEWIACIFPGFGITNYANSVKGRFTISSDS AQNTVFLQMTSLTASDTATYFCAREYGSPSGYYGVGY HSPLWGPGLTVTVSS
	VL	46	AAVLTQTSPVSAAVGGTVSISCQSSQSVYKNNWLSW FQQKPGQRPKLLIYAASNLESGVPSRFSGSGSGTQFT LTISDVQCDDAATYYCAGGYSSSSDYAFGGGTEVVVK

mAb	IgG chain	SEQ ID	Amino acid sequence
6O11	VH	248	QSLEESGGDLVKPGASLTLTCTASGFSFSSSYWICWV RQAPGKGLELIGCINSGSGFTYYASWVNGRFTGSKTS STTVTLQMTSLTAADTATYFCARAGNDGWGEDLWGP TLVTVSS
	VL	249	DIVMTQTPASVSEPVGGTVTIKCQASQSIYSYCSWYQ QKPGQPPKRLIYYASTLASGVPSRFEGSGSGTEFTLT ISDLECAATAATYYCQNNNGVNGRGTFFGGGTEVVVK

Table 26. Amino acid sequences of full-length antibody chains for anti-VCP antibodies

mAb	IgG chain	SEQ ID	Amino acid sequence
11G6	Heavy chain	47	QEQLVESGGGLVQPGESLKLCKVSGIDLSYYGVSWV RQAPGKGPEWIACIFPGFGITNYANSVKGRFTISSDS AQNTVFLQMTSLTASDTATYFCAREYGSPPGYGVGY HSPWGPGLTVTVSSASTKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS SGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDK KVEPKSCDKHTCTCPPCPAPELGGPSVFLFPPKPKDT LMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNA KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVS NKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKN QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVL DSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNH YTQKSLSLSPGK
	Light chain	48	AAVLTQTPSPVSAAVGGTVSTISCQSSQSVYKNNWLSW FQQKPGQRPKLLIYAASNLESGVPSRFSGSGSGTQFT LTISDVQCDDAATYYCAGGYSSSSDYAFGGGTEVVVK RTVAAPSVFIFPPSDEQLKSGTASVVCILNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDSSTYSLSSTLT SKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

mAb	IgG chain	SEQ ID	Amino acid sequence
6O11	Heavy chain	250	QSLEESGGDLVKPGASLTLTCTASGFSFSSSYWICWV RQAPGKGLELIGCINSGSGFTYYASWVNGRFTGSKTS STTVTLQMTSLTAADTATYFCARAGNDGWGEDLWGP TLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVK DYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSS VVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD KTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQ YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV KGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL YSKLTVDKSRWQQGNVFSQSVMEALHNHYTQKSLSL SPGK
	Light chain	251	DIVMTQTPASVSEFVGGTVTIKCQASQSIVSYCSWYQ QKPGQPPKRLIYYASTLASGVPSRFEGSGSGTEFTLT ISDLECAAAATYYCQNNNGVNGRGT PFGGGTEVVVKR TVAAPSVFIFPPSDEQLKSGTASVVCCLNNFYPREAK VQWKVDNALQSGNSQESVTEQDSKSTYLSSTLTLS KADYEEKHKVYACEVTHQGLSSPVTKSFNRGEC

Table 27. Nucleic acid sequences of full-length antibody chains for anti-VCP antibodies

mAb	IgG chain	SEQ ID	Nucleic acid sequence
11G6	Heavy chain	87	CAGGAGCAGCTGGTGGAGTCTGGAGGGGGTCTGGTCCAGCCGGGGGAA TCCCTGAAACTCTCCTGCAAAGTCTCTGGAATCGACCTCAGTTACTAT GGAGTGAGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGAGTGGATC GCTTGCACTTTTCTGGTTTTGGTATCACAACCTACGCGAAGTCTGTG AAGGGCCGATTCAACCATCTCCAGCGACAGCGCCAGAACACGGTGTTT CTGCAAATGACCAGTCTGACAGCCTCGGACACGGCCACCTATTCTGT GCAAGAGAGTATGGTAGTCTTAGTGGTTATTATGGGGTAGGTTATCAC TCTCCCTTATGGGGCCAGGCACCTGGTCACCGTCTCCTCAGCATCC ACCAAGGGCCCATCGGTCTTCCCCCTGGCACCTCTCCAAGAGCACC TCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCC GAACCGGTGACGGTGTCTGTGGAATCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTACAGTCTCAGGACTCTACTCCCTCAGC AGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATC TGCAACGTGAATCACAAGCCAGCAACACCAAGGTGGACAAGAAAGTT GAGCCCAAATCTGTGACAAAACCTCACACATGCCACCGTGCCAGCA

mAb	IgG chain	SEQ ID	Nucleic acid sequence
			CCTGAACCTCCTGGGGGACCGTCAGTCTTCCTCTTCCCCCAAACCC AAGGACACCCCTCATGATCTCCCGACCCCTGAGGTCACATGCGTGGTG GTGGACGTGAGCCACGAAGACCCCTGAGGTCAAGTTCAACTGGTACGTG GACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCCGGGAGGAGCAG TACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCCTCCTGCACCAG GACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCC CTCCCAGCCCCCATCGAGAAAACCATCTCCAAGGCCAAAGGGCAGCCC CGAGAACACAGGTGTACACCTGCCCCCATCCCGGATGAGCTGACC AAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGC GACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACCTAC AAGACCAGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCTATAT TCAAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTC TCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAG AGCCTCTCCCTGTCTCCCGGAAA
	Light chain	88	GCCGCCGTGCTGACCCAGACTCCATCTCCCGTGTCTGCAGCTGTGGGA GGCACAGTCAGCATCAGTTGCCAGTCCAGTCAGAGTGTTTATAAGAAC AACTGGTTATCCTGGTTTCAGCAGAAACCAGGGCAGCGTCCCAGCTC CTGATCTATGCTGCATCCAATCTGGAATCTGGGGTCCCATCGCGCTTC AGCGGCAGTGGATCTGGGACACAGTTCACTCTCACCATCAGCGACGTG CAGTGTGACGATGCTGCCACTTACTACTGTGCAGGCGGTTATAGTAGT AGTAGTGATTATGCTTTCGGCGGAGGACCGAGGTGGTCTGTCAAACGA ACTGTGGCTGCACCATCTGTCTTCATCTTCCCGCCATCTGATGAGCAG TTGAAATCTGGAAGTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGAAGGTGGATAACGCCCTCCAATCG GGTAACTCCCAGGAGAGTGTACAGAGCAGGACAGCAAGGACAGCACC TACAGCCTCAGCAGCACCCTGACGCTGAGCAAAGCAGACTACGAGAAA CACAAAGTCTACGCCCTGCGAAGTCACCCATCAGGGCCTGAGCTCGCCC GTCACAAAGAGCTTCAACAGGGGAGAGTGT
6O11	Heavy chain	252	CAGTCGTTGGAGGAGTCCGGGGGAGACCTGGTCAAGCCTGGGGCATCC CTGACACTCACCTGCACAGCCTCTGGATTCTCCTTCAGTAGCAGCTAC TGGATATGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTTGATC GGATGCATTAATAGTGGTAGTGGTTTTACATACTACGCGAGCTGGGTG AATGGCCGATTCACCGGCTCCAAAACCTCGTCGACCACGGTGACTCTG CAAATGACCAGTCTGACAGCCGCGGACACGGCCACCTATTTCTGTGCG AGAGCGGAAATGATGGGTGGGGTGAGGACTTGTGGGGCCAGGCACC CTGGTCACCGTCTCCTCAGCATCCACCAAGGGCCCATCGGTCTTCCC CTGGCACCCCTCCTCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGC TGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCTGTGAAC

mAb	IgG chain	SEQ ID	Nucleic acid sequence
			TCAGGCGCCCTGACCAGCGGCGTGACACCTTCCCGGCTGTCCTACAG TCCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGC AGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGC AACACCAAGGTGGACAAGAAAGTTGAGCCCAAATCTTGTGACAAAAC CACACATGCCCACCGTGCCAGCACCTGAATCCTGGGGGACCGTCA GTCTTCTCTTCCCCCAAACCCAAGGACACCTCATGATCTCCCGG ACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCT GAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCC AAGACAAAGCCGCGGAGGAGCAGTACAACAGCACGTACCGTGTGGTC AGCGTCTCACCCTCTGCACCAGGACTGGCTGAATGGCAAGGAGTAC AAGTGCAAGGTCTCCAACAAGCCCTCCAGCCCCATCGAGAAAACC ATCTCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTG CCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTGAGCCTGACCTGC CTGGTCAAAGGCTTCTATCCAGCGACATCGCCGTGGAGTGGGAGAGC AATGGGCAGCCGAGAACAACTACAAGACCACGCCTCCCGTGTGGAC TCCGACGGCTCCTTCTTCTTATATCAAGCTCACCGTGGACAAGAGC AGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCT CTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCCGGGAAA
	Light chain	253	GACATTGTGATGACCCAGACTCCAGCCTCCGTGTCTGAACCTGTGGGA GGCACAGTCACCATCAAGTGCCAGGCCAGTCAGAGCATTGTTAGTTAC TGTTCTTGGTATCAGCAGAAACCAGGGCAGCCTCCCAAGCGCTGATC TATTATGCATCCACTCTGGCATCTGGGGTCCCATCGCGGTTCAAGGC AGTGGATCTGGGACAGAGTTCACTCTCACCATCAGCGACCTGGAGTGT GCCGATGCTGCCACTTACTACTGTCAAACAATAATGGTGTTAATGGT CGTGGAACCTCTTTCGGCGGAGGGACCGAGGTGGTGGTCAAACGAAC GTGGCTGCACCATCTGTCTTCATCTTCCCGCCATCTGATGAGCAGTTG AAATCTGGAACCTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTATCCC AGAGAGGCCAAAGTACAGTGAAGGTGGATAACGCCCTCCAATCGGGT AACTCCCAGGAGAGTGTACAGAGCAGGACAGCAAGGACAGCACCTAC AGCCTCAGCAGCACCTGACGCTGAGCAAAGCAGACTACGAGAAACAC AAAGTCTACGCTGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTC ACAAAGAGCTTCAACAGGGGAGAGTGT

[00257] In some embodiments, the sequences of the heavy chain variable domains, light chain variable domains, full-length heavy chains, and full-length light chains may be “mixed and matched” to create variants of the anti-VCP antibodies. Such “mixed and matched” anti-VCP antibodies can be tested using binding assays known in the art (*e.g.*, ELISAs and other

assays described in the Examples). In various embodiments, an anti-VCP antibody or antigen binding fragment disclosed herein may comprise any set of heavy and light chain variable domains listed in Table 25 above, or the set of six CDR sequences from the heavy and light chain set. In some embodiments, an antibody or antigen-binding fragment further comprise human heavy and light chain constant domains or fragments thereof. In some embodiments, an anti-VCP antibody may comprise a human IgG heavy chain constant domain and a human kappa light chain constant domain. In some embodiments, the anti-VCP antibody may comprise a human IgG1, IgG2, IgG3, or IgG4 heavy chain constant domain. In various embodiments, an anti-VCP antibody of the present invention comprises a human immunoglobulin G subtype 1 (IgG1) heavy chain constant domain with a human Ig kappa light chain constant domain. In various embodiments, an anti-VCP antibody may comprise any set of full-length heavy chain and full-length light chain sequences listed in Table 26 above.

[00258] In some embodiments, an anti-VCP antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 33 (HCDR1), SEQ ID NO: 34 (HCDR2), and SEQ ID NO: 35 (HCDR3); and three LCDRs comprising SEQ ID NO: 36 (LCDR1), SEQ ID NO: 37 (LCDR2), and SEQ ID NO: 38 (LCDR3) as defined by the Kabat numbering system.

[00259] In some embodiments, an anti-VCP antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 39 (HCDR1), SEQ ID NO: 40 (HCDR2), and SEQ ID NO: 41 (HCDR3); and three LCDRs comprising SEQ ID NO: 42 (LCDR1), SEQ ID NO: 43 (LCDR2), and SEQ ID NO: 38 (LCDR3) as defined by the IMGT numbering system.

[00260] In some embodiments, an anti-VCP antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 159 (HCDR1), SEQ ID NO: 240 (HCDR2), and SEQ ID NO: 241 (HCDR3); and three LCDRs comprising SEQ ID NO: 242 (LCDR1), SEQ ID NO: 209 (LCDR2), and SEQ ID NO: 243 (LCDR3) as defined by the Kabat numbering system.

[00261] In some embodiments, an anti-VCP antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 164 (HCDR1), SEQ ID NO: 244 (HCDR2), and SEQ ID NO: 245 (HCDR3); and three LCDRs comprising

SEQ ID NO: 246 (LCDR1), SEQ ID NO: 215 (LCDR2), and SEQ ID NO: 243 (LCDR3) as defined by the IMGT numbering system.

[00262] In some embodiments, an anti-VCP antibody or antigen-binding fragment comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 45, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 46.

[00263] In some embodiments, an anti-VCP antibody or antigen-binding fragment comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 248, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 249.

[00264] In some embodiments, an anti-VCP antibody or antigen-binding fragment thereof provided herein comprises three HCDRs from the heavy chain variable region comprising SEQ ID NO: 45, and three LCDRs from the light chain variable region comprising SEQ ID NO: 46. In some embodiments, an anti-VCP antibody or antigen-binding fragment thereof provided herein comprises three HCDRs from the heavy chain variable region comprising SEQ ID NO: 248, and three LCDRs from the light chain variable region comprising SEQ ID NO: 249.

[00265] In some embodiments, an anti-VCP antibody or antigen-binding fragment thereof provided herein comprises a heavy chain variable region with at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 45. In some embodiments, an anti-VCP antibody or antigen-binding fragment thereof provided herein comprises a heavy chain variable region with at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 248.

[00266] In some embodiments, an anti-VCP antibody or antigen-binding fragment thereof provided herein comprises a light chain variable region with at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 46. In some embodiments, an anti-eribulin antibody or antigen-binding fragment thereof provided herein comprises a light chain variable region with at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at

least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to SEQ ID NO: 249.

[00267] In various embodiments, an anti-VCP antibody comprises a human IgG heavy chain constant domain. In some embodiments, the IgG heavy chain constant domain is IgG1.

[00268] In various embodiments, an anti-VCP antibody comprise a human Ig kappa light chain constant region. In various embodiments, the anti-VCP antibody comprise a human Ig lambda light chain constant region.

[00269] In some embodiments, an anti-VCP antibody or antigen-binding fragment provided herein comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 47. In some embodiments, an anti-VCP antibody or antigen-binding fragment thereof provided herein comprises a light chain comprising an amino acid sequence of SEQ ID NO: 48.

[00270] In some embodiments, an anti-eribulin antibody or antigen-binding fragment provided herein comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 250. In some embodiments, an anti-VCP antibody or antigen-binding fragment thereof provided herein comprises a light chain comprising an amino acid sequence of SEQ ID NO: 251.

[00271] In some embodiments, an anti-VCP antibody or antigen-binding fragment provided herein is antibody 11G6.

[00272] In some embodiments, an anti-VCP antibody or antigen-binding fragment provided herein is conjugated to a label. In some embodiments, the anti-VCP antibody or antigen-binding fragment is conjugated to a fluorescent tag. In some embodiments, the anti-VCP antibody or antigen-binding fragment is conjugated to a biotin moiety. In some embodiments, the anti-VCP antibody or antigen-binding fragment is conjugated to a streptavidin moiety. In some embodiments, the anti-VCP antibody or antigen-binding fragment is conjugated to an enzyme reporter. In some embodiments, the anti-VCP antibody or antigen-binding fragment is conjugated to a bead. In some embodiments, the bead is an agarose bead or a magnetic bead. In some embodiments, the anti-VCP antibody or antigen-binding fragment is conjugated to a luminescent tag. In some embodiments, the anti-VCP antibody or antigen-binding fragment is conjugated to an electrochemiluminescent tag.

[00273] In some embodiments, an anti-VCP antibody or antigen-binding fragment provided herein is conjugated to a fluorescent tag.

[00274] In some embodiments, an anti-VCP antibody or antigen-binding fragment provided herein is conjugated to a luminescent tag.

[00275] In some embodiments, an anti-VCP antibody or antigen-binding fragment provided herein is conjugated to an electrochemiluminescent tag.

[00276] In some embodiments, an anti-VCP antibody or antigen binding fragment specifically binds a linker-payload conjugate comprising VCP. In some embodiments, an anti-VCP antibody or antigen binding fragment specifically binds a linker-payload conjugate comprising VCP-eribulin. In some embodiments, an anti-VCP antibody or antigen binding fragment specifically binds a linker-payload conjugate comprising Mal-(PEG)_m-VCP-eribulin, wherein *m* is an integer from 1 to 10. In some embodiments, the linker-payload conjugate comprises Mal-(PEG)₂-VCP-eribulin.

Methods For Detecting Antibody-Drug Conjugate Metabolites

[00277] In designing efficacious ADC therapies, it is beneficial to evaluate the clinical pharmacology of the ADC, including quantifying the ADC and its constituent parts in circulation after administration of an ADC to a subject. In some embodiments, an ADC administered to a subject may release metabolites in circulation.

[00278] An ADC may metabolize in circulation via a variety of pathways (FIG. 1). Exemplary ADC metabolites include an antibody or antigen-binding fragment, linker-payload conjugate, linker-payload conjugated to albumin, free payload, and linker unconjugated to either ADC or payload. Accurate measurement of pharmacologically active metabolites in systemic circulation may inform exposure-response analyses. Such analyses may assist in evaluating efficacious dose selection in a subject or likelihood of side effects from dosing.

[00279] The methods disclosed herein describe novel antibodies, as well as immunodepletion methods for quantifying ADC metabolites. To quantify potential ADC metabolites, an assay or assays may measure one or more of free payload, total ADC and/or antibody or antigen-binding fragment, intact ADC, and linker-payload conjugate. In some embodiments, a method disclosed herein measures intact ADC in a DAR-insensitive manner. In some embodiments, a method disclosed herein measures intact ADC in a DAR-sensitive manner.

[00280] In some embodiments, the methods disclosed herein are performed using a biological sample obtained from a subject. In some embodiments, the biological sample

comprises whole blood, plasma, and/or serum. In some embodiments, the biological sample comprises plasma.

[00281] In some embodiments, the biological sample used in any assay described herein is obtained from a subject after administration of an ADC. In some embodiments, the ADC comprises an anti-FRA antibody or antigen-binding fragment. In some embodiments, the ADC comprises farletuzumab. In some embodiments, the ADC comprises MORAb-202. In some embodiments, the ADC comprises an anti-MSLN antibody or antigen-binding fragment. In some embodiments, the ADC comprises 345A12. In some embodiments, the ADC comprises MORAb-109. In some embodiments, the ADC comprises an anti-HER2 antibody or antigen-binding fragment. In some embodiments, the ADC comprises trastuzumab.

[00282] In some embodiments, the methods disclosed herein comprise an immunoassay. In some embodiments, the immunoassay comprises an antibody conjugated to a label. Methods for conjugating labels to an antibody are known in the art and include, for example, covalent attachment of the label to an antibody (e.g., using succinimide, e.g., NHS, conjugation to lysine, maleimide conjugation to cysteine, or click chemistry to introduce azide or alkyne structures). In some embodiments, the label comprises a streptavidin or bead. In some embodiments, the antibody is immobilized on a solid support. In some embodiments, the label is detectable. In some embodiments, the method comprises detecting a signal from a labeled antibody. "Detecting a signal" may comprise quantifying information from a detectably labeled antibody using any method known in the art. Exemplary signals include fluorescence, luminescence, or electrochemiluminescence. Exemplary detection methods include microfluidic immunoassay detection (e.g., Gyros xPand), flow cytometry, spectrophotometry, and fluorescence microscopy. Any method known in the art for translating signal data into quantification of a target may be used, including reference to standards.

[00283] In various embodiments, disclosed herein are methods for detecting a metabolite of an antibody-drug conjugate. Further details regarding assays for measuring ADC metabolites are enumerated below.

Quantifying Free Payload

[00284] In some embodiments, a method for detecting a metabolite of an ADC comprises an assay to quantify free payload. In some embodiments, free payload in a biological sample is quantified. In some embodiments, the biological sample is plasma. Methods for quantifying free payload are known in the art and include, for example, solid phase extraction followed by liquid-chromatography/mass spectrometry or multiple reaction monitoring.

[00285] In some embodiments, the free payload is eribulin. In some embodiments, the eribulin is quantified in a plasma sample from a subject administered an ADC. In some embodiments, the ADC comprises an anti-FRA antibody or antigen-binding fragment. In some embodiments, the ADC comprises farletuzumab. In some embodiments, the ADC comprises MORAb-202. In some embodiments, the ADC comprises an anti-MSLN antibody or antigen-binding fragment. In some embodiments, the ADC comprises 345A12. In some embodiments, the ADC comprises MORAb-109. In some embodiments, the ADC comprises an anti-HER2 antibody or antigen-binding fragment. In some embodiments, the ADC comprises trastuzumab.

[00286] In some embodiments, the limit of quantification (LOQ) of eribulin in a plasma sample is at least 5 pg/ml, at least 10 pg/ml, at least 15 pg/ml, at least 20 pg/ml, at least 25 pg/ml, or at least 30 pg/ml as determined by multiple reaction monitoring (MRM). In some embodiments, the LOQ of eribulin in a plasma sample is at least 10 pg/ml as determined by MRM.

Quantifying Total Antibody/ADC

[00287] In some embodiments, a method for detecting a metabolite of an ADC comprises an assay to quantify total ADC and/or antibody or antigen-binding fragment. In some embodiments, total ADC and/or antibody or antigen-binding fragment is quantified in a biological sample. In some embodiments, the biological sample is plasma. In some embodiments, total ADC and/or antibody or antigen-binding fragment in sample is quantified using an anti-idiotypic antibody, e.g., an anti-idiotypic antibody against an FRA, MSLN, or HER2 antibody or antigen binding fragment (also referred to herein as an anti-FRA idiotype antibody or antigen-binding fragment, anti-MSLN idiotype antibody or antigen-binding fragment, or anti-HER2 idiotype antibody or antigen-binding fragment).

[00288] Methods for quantifying total ADC and/or antibody or antigen-binding fragment concentration are known in the art and include, for example, a sandwich immunoassay, e.g.,

ELISA, fluorescence, luminescence, and electrochemiluminescence. An exemplary method disclosed herein quantifies total ADC and/or antibody or antigen-binding fragment using fluorescent detection in a sandwich immunoassay. Sandwich immunoassays are known in the art and comprise a first step wherein an antigen is captured by a first antibody immobilized on a fixed surface, and a second step wherein the antigen is detected by binding with a second antibody conjugated to a detectable label.

[00289] In some embodiments, the sandwich immunoassay comprises a first antibody (“capture antibody”) and a second antibody (“detection antibody”). In some embodiments, the capture antibody is biotinylated. In some embodiments, the detection antibody is conjugated to a detectable label. In some embodiments, the detectable label is a fluorescent label.

[00290] In some embodiments, the assay quantifies total ADC and/or antibody or antigen-binding fragment, wherein the ADC and/or antibody or antigen-binding fragment specifically bind folate receptor alpha. In some embodiments, the ADC is MORAb-202. In some embodiments, the antibody is farletuzumab or an antigen-binding fragment thereof. In some embodiments, the antibody or antigen-binding fragment comprises three heavy chain CDRs and three light chain CDRs as follows: HCDR1 comprising SEQ ID NO: 49, HCDR2 comprising SEQ ID NO: 50, HCDR3 comprising SEQ ID NO: 51; LCDR1 comprising SEQ ID NO: 52, LCDR2 comprising SEQ ID NO: 53, and LCDR3 comprising SEQ ID NO: 54, as defined by the Kabat numbering system. In some embodiments, the antibody or antigen-binding fragment comprises three heavy chain CDRs and three light chain CDRs as follows: HCDR1 comprising SEQ ID NO: 55, HCDR2 comprising SEQ ID NO: 56, HCDR3 comprising SEQ ID NO: 57; LCDR1 comprising SEQ ID NO: 58, LCDR2 comprising SEQ ID NO: 59, and LCDR3 comprising SEQ ID NO: 60, as defined by the IMGT numbering system. In some embodiments, the antibody or antigen-binding fragment comprises a heavy chain variable domain comprising a sequence of SEQ ID NO: 61 and a light chain variable domain comprising a sequence of SEQ ID NO: 62. In some embodiments, the antibody or antigen-binding fragment comprises a heavy chain of SEQ ID NO: 63 and a light chain sequence of SEQ ID NO: 64.

[00291] In some embodiments, the capture antibody or antigen-binding fragment is an anti-FRA idiotypic antibody or antigen-binding fragment. In some embodiments, the capture antibody or antigen-binding fragment is an anti-farletuzumab antibody or antigen-binding

fragment. In some embodiments, the capture antibody or antigen-binding fragment is 2G9. In some embodiments, the capture antibody is an antigen-binding Fab fragment, e.g., a Fab fragment of 2G9. In some embodiments, the capture antibody is a Fab2 antigen-binding fragment. In some embodiments, the capture antibody is biotinylated. In some embodiments the capture antibody is immobilized on a solid support. In some embodiments, the detection antibody or antigen-binding fragment is an anti-human IgG Fc antibody or antigen-binding fragment. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment binds the CH2 domain. In some embodiments, the detection antibody or antigen-binding fragment is an anti-farletuzumab antibody or antigen-binding fragment. In some embodiments, the detection antibody or antigen-binding fragment is 2G9. In some embodiments, the detection antibody or antigen-binding fragment is an anti-FRA idiotypic antibody or antigen-binding fragment. In some embodiments, the detection antibody or antigen-binding fragment is immobilized on a solid support. In some embodiments, the detection antibody is conjugated to a fluorescent tag.

[00292] In some embodiments, the assay quantifies total ADC and/or antibody or antigen-binding fragment, wherein the ADC and/or antibody or antigen-binding fragment specifically binds mesothelin. In some embodiments, the ADC is MORAb-109. In some embodiments, the antibody is 345A12 or an antigen-binding fragment thereof. In some embodiments, the antibody or antigen-binding fragment comprises three heavy chain CDRs and three light chain CDRs as follows: HCDR1 comprising SEQ ID NO: 65, HCDR2 comprising SEQ ID NO: 66, HCDR3 comprising SEQ ID NO: 67; LCDR1 comprising SEQ ID NO: 68, LCDR2 comprising SEQ ID NO: 69, and LCDR3 comprising SEQ ID NO: 70, as defined by the Kabat numbering system. In some embodiments, the antibody or antigen-binding fragment comprises three heavy chain CDRs and three light chain CDRs as follows: HCDR1 comprising SEQ ID NO: 71, HCDR2 comprising SEQ ID NO: 72, HCDR3 comprising SEQ ID NO: 73; LCDR1 comprising SEQ ID NO: 74, LCDR2 comprising SEQ ID NO: 75, and LCDR3 comprising SEQ ID NO: 76, as defined by the IMGT numbering system. In some embodiments, the antibody or antigen-binding fragment comprises a heavy chain variable domain comprising a sequence of SEQ ID NO: 77 and a light chain variable domain comprising a sequence of SEQ ID NO: 78. In some embodiments, the antibody or antigen-binding fragment comprises a heavy chain of SEQ ID NO: 79 and a light chain sequence of SEQ ID NO: 80.

[00293] In some embodiments, the capture antibody or antigen-binding fragment is an anti-MSLN idiotypic antibody or antigen-binding fragment. In some embodiments, the capture antibody or antigen-binding fragment is an anti-345A12 antibody or antigen-binding fragment. In some embodiments, the capture antibody or antigen-binding fragment is an antigen-binding Fab fragment. In some embodiments, the capture antibody or antigen-binding fragment is a Fab2 antigen-binding fragment. In some embodiments, the capture antibody or antigen-binding fragment is biotinylated. In some embodiments, the capture antibody is immobilized on a solid support. In some embodiments, the detection antibody or antigen-binding fragment is an anti-human IgG Fc antibody or antigen-binding fragment. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment binds the CH2 domain. In some embodiments, the detection antibody or antigen-binding fragment is an anti-345A12 antibody or antigen-binding fragment. In some embodiments, the detection antibody or antigen-binding fragment is an anti-MSLN idiotypic antibody or antigen-binding fragment. In some embodiments, the detection antibody or antigen-binding fragment is immobilized on a solid support. In some embodiments, the detection antibody is conjugated to a fluorescent tag.

[00294] In some embodiments, the assay quantifies total ADC and/or antibody or antigen-binding fragment, wherein the ADC and/or antibody or antigen-binding fragment specifically binds HER2. In some embodiments, the antibody is trastuzumab or an antigen-binding fragment thereof. In some embodiments, the antibody or antigen-binding fragment comprises three heavy chain CDRs and three light chain CDRs as follows: HCDR1 comprising SEQ ID NO: 254, HCDR2 comprising SEQ ID NO: 255, HCDR3 comprising SEQ ID NO: 256; LCDR1 comprising SEQ ID NO: 257, LCDR2 comprising SEQ ID NO: 258, and LCDR3 comprising SEQ ID NO: 259, as defined by the Kabat numbering system. In some embodiments, the antibody or antigen-binding fragment comprises three heavy chain CDRs and three light chain CDRs as follows: HCDR1 comprising SEQ ID NO: 260, HCDR2 comprising SEQ ID NO: 261, HCDR3 comprising SEQ ID NO: 262; LCDR1 comprising SEQ ID NO: 263, LCDR2 comprising SEQ ID NO: 264, and LCDR3 comprising SEQ ID NO: 265, as defined by the IMGT numbering system. In some embodiments, the antibody or antigen-binding fragment comprises a heavy chain variable domain comprising a sequence of SEQ ID NO: 266 and a light chain variable domain comprising a sequence of SEQ ID NO:

267. In some embodiments, the antibody or antigen-binding fragment comprises a heavy chain of SEQ ID NO: 268 and a light chain sequence of SEQ ID NO: 269.

[00295] In some embodiments, the capture antibody or antigen-binding fragment is an anti-HER2 idiotypic antibody or antigen-binding fragment. In some embodiments, the capture antibody or antigen-binding fragment is an anti-trastuzumab antibody or antigen-binding fragment. In some embodiments, the capture antibody or antigen-binding fragment is an antigen-binding Fab fragment, e.g., an anti-trastuzumab antigen-binding Fab fragment. In some embodiments, the capture antibody or antigen-binding fragment is a Fab2 antigen-binding fragment. In some embodiments, the capture antibody or antigen-binding fragment is biotinylated. In some embodiments, the capture antibody is immobilized on a solid support. In some embodiments, the detection antibody or antigen-binding fragment is an anti-HER2 idiotypic antibody or antigen-binding fragment. In some embodiments, the detection antibody is an anti-trastuzumab antibody or antigen-binding fragment. In some embodiments, the detection antibody or antigen-binding fragment is an antigen-binding Fab fragment. In some embodiments, the detection antibody or antigen-binding fragment is immobilized on a solid support. In some embodiments, the detection antibody or antigen-binding fragment is conjugated to a fluorescent tag.

Quantifying Intact ADC (DAR insensitive and DAR sensitive)

[00296] In some embodiments, a method for detecting a metabolite of an ADC comprises an assay to quantify intact ADC. In some embodiments, intact ADC is quantified in a biological sample. In some embodiments, the biological sample is plasma. In some embodiments, the assay is a sandwich immunoassay. An exemplary method disclosed herein quantifies intact ADC using fluorescent detection in a sandwich immunoassay.

[00297] In some embodiments, the sandwich immunoassay comprises a first antibody (“capture antibody”) and a second antibody (“detection antibody”). In some embodiments, the capture antibody is biotinylated. In some embodiments, the detection antibody is conjugated to a detectable label. In some embodiments, the detectable label is a fluorescent label.

[00298] In some embodiments, the intact ADC assay quantifies an intact ADC, wherein the ADC specifically binds FRA. In some embodiments, the intact ADC is MORAb-202. In some embodiments, the intact ADC comprises farletuzumab or an antigen-binding fragment

thereof. In some embodiments, the intact ADC comprises an antibody comprising three heavy chain CDRs and three light chain CDRs as follows: HCDR1 comprising SEQ ID NO: 49, HCDR2 comprising SEQ ID NO: 50, HCDR3 comprising SEQ ID NO: 51; LCDR1 comprising SEQ ID NO: 52, LCDR2 comprising SEQ ID NO: 53, and LCDR3 comprising SEQ ID NO: 54, as defined by the Kabat numbering system. In some embodiments, the intact ADC comprises an antibody comprising three heavy chain CDRs and three light chain CDRs as follows: HCDR1 comprising SEQ ID NO: 55, HCDR2 comprising SEQ ID NO: 56, HCDR3 comprising SEQ ID NO: 57; LCDR1 comprising SEQ ID NO: 58, LCDR2 comprising SEQ ID NO: 59, and LCDR3 comprising SEQ ID NO: 60, as defined by the IMGT numbering system. In some embodiments, the intact ADC comprises an antibody comprising a heavy chain variable domain comprising a sequence of SEQ ID NO: 61 and a light chain variable domain comprising a sequence of SEQ ID NO: 62. In some embodiments, the intact ADC comprises an antibody comprising a heavy chain of SEQ ID NO: 63 and a light chain sequence of SEQ ID NO: 64. In some embodiments, the intact ADC has a DAR of 4. In some embodiments, the intact ADC has a DAR of 2.

[00299] In some embodiments, the intact ADC assay quantifies an intact ADC, wherein the ADC specifically binds MSLN. In some embodiments, the intact ADC is MORAb-109. In some embodiments, the intact ADC comprises 345A12 or an antigen-binding fragment thereof. In some embodiments, the intact ADC comprises an antibody comprising three heavy chain CDRs and three light chain CDRs as follows: HCDR1 comprising SEQ ID NO: 65, HCDR2 comprising SEQ ID NO: 66, HCDR3 comprising SEQ ID NO: 67; LCDR1 comprising SEQ ID NO: 68, LCDR2 comprising SEQ ID NO: 69, and LCDR3 comprising SEQ ID NO: 70, as defined by the Kabat numbering system. In some embodiments, the intact ADC comprises an antibody comprising three heavy chain CDRs and three light chain CDRs as follows: HCDR1 comprising SEQ ID NO: 71, HCDR2 comprising SEQ ID NO: 72, HCDR3 comprising SEQ ID NO: 73; LCDR1 comprising SEQ ID NO: 74, LCDR2 comprising SEQ ID NO: 75, and LCDR3 comprising SEQ ID NO: 76, as defined by the IMGT numbering system. In some embodiments, the intact ADC comprises an antibody comprising a heavy chain variable domain comprising a sequence of SEQ ID NO: 77 and a light chain variable domain comprising a sequence of SEQ ID NO: 78. In some embodiments, the intact ADC comprises an antibody comprising a heavy chain of SEQ ID

NO: 79 and a light chain sequence of SEQ ID NO: 80. In some embodiments, the intact ADC has a DAR of 4. In some embodiments, the intact ADC has a DAR of 2.

[00300] In some embodiments, the intact ADC assay quantifies an intact ADC, wherein the ADC specifically binds HER2. In some embodiments, the intact ADC comprises trastuzumab or an antigen-binding fragment thereof. In some embodiments, the intact ADC comprises an antibody comprising three heavy chain CDRs and three light chain CDRs as follows: HCDR1 comprising SEQ ID NO: 254, HCDR2 comprising SEQ ID NO: 255, HCDR3 comprising SEQ ID NO: 256; LCDR1 comprising SEQ ID NO: 257, LCDR2 comprising SEQ ID NO: 258, and LCDR3 comprising SEQ ID NO: 259, as defined by the Kabat numbering system. In some embodiments, the intact ADC comprises an antibody comprising three heavy chain CDRs and three light chain CDRs as follows: HCDR1 comprising SEQ ID NO: 260, HCDR2 comprising SEQ ID NO: 261, HCDR3 comprising SEQ ID NO: 262; LCDR1 comprising SEQ ID NO: 263, LCDR2 comprising SEQ ID NO: 264, and LCDR3 comprising SEQ ID NO: 265, as defined by the IMGT numbering system. In some embodiments, the intact ADC comprises an antibody comprising a heavy chain variable domain comprising a sequence of SEQ ID NO: 266 and a light chain variable domain comprising a sequence of SEQ ID NO: 267. In some embodiments, the intact ADC comprises an antibody comprising a heavy chain of SEQ ID NO: 268 and a light chain sequence of SEQ ID NO: 269. In some embodiments, the intact ADC has a DAR of 4. In some embodiments, the intact ADC has a DAR of 2.

[00301] In various embodiments, the intact ADC assay is DAR insensitive. In some embodiments, a capture antibody or antigen-binding fragment in a DAR insensitive assay is an anti-eribulin antibody or antigen-binding fragment as disclosed herein. In some embodiments, the capture antibody or antigen-binding fragment is 5E4. In some embodiments, the capture antibody or antigen-binding fragment is an antigen-binding fragment. In some embodiments, the capture antigen-binding fragment is a Fab fragment. In some embodiments, the capture antibody or antigen-binding fragment is biotinylated. In some embodiments, the capture antibody or antigen-binding fragment is immobilized on a solid support. In some embodiments, the detection antibody or antigen-binding fragment is an anti-ID antibody or antigen-binding fragment. In some embodiments, the detection antibody or antigen-binding fragment is an anti-human IgG Fc antibody or antigen-binding fragment. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment binds the CH2 domain. In some embodiments, the detection antibody or antigen-binding fragment is

conjugated to a detectable label. In some embodiments, the detectable label is a fluorescent tag.

[00302] In some embodiments, a method for detecting intact ADC in a DAR insensitive manner is provided herein. In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered an ADC. In some embodiments, the method further comprises contacting the biological sample with 5E4. In some embodiments, the 5E4 is a Fab fragment. In some embodiments, the 5E4 is biotinylated. In some embodiments, 5E4 is immobilized on a solid support. In some embodiments, the method further comprises contacting the biological sample with an anti-ID antibody or antigen-binding fragment or with an anti-human IgG Fc antibody or antigen-binding fragment. In some embodiments, the anti-ID antibody or antigen-binding fragment and/or the anti-human IgG Fc antibody or antigen-binding fragment is conjugated to a detectable label, e.g., a fluorescent tag. In some embodiments, a signal from the detectable label is detected for quantification of the intact ADC. In some embodiments, the anti-ID antibody is 2G9 or an antigen-binding fragment thereof. In some embodiments, the anti-ID antibody is an anti-345A12 idiotype antibody or antigen-binding fragment thereof. In some embodiments, the intact ADC is MORAb-202. In some embodiments, the intact ADC is MORAb-109.

[00303] In some embodiments, the DAR insensitive assay quantifies an intact anti-FRA ADC. In some embodiments, the capture antibody or antigen-binding fragment is an anti-eribulin antibody or antigen-binding fragment as disclosed herein. In some embodiments, the capture antibody or antigen-binding fragment is 5E4. In some embodiments, the 5E4 is an antigen-binding fragment. In some embodiments, the 5E4 is a Fab fragment. In some embodiments, the 5E4 is biotinylated. In some embodiments, the 5E4 is immobilized on a solid support. In some embodiments, the detection antibody or antigen-binding fragment is an anti-ID antibody or antigen-binding fragment. In some embodiments, the anti-ID antibody or antigen-binding fragment is 2G9. In some embodiments, the 2G9 is conjugated to a detectable label. In some embodiments, the detectable label is a fluorescent tag. In some embodiments, the detection antibody or antigen-binding fragment is an anti-human IgG Fc antibody or antigen-binding fragment. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment binds the CH2 domain. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment is conjugated to a detectable label. In some embodiments, the detectable label is a fluorescent tag.

[00304] In some embodiments, the DAR insensitive assay quantifies an intact anti-MSLN ADC. In some embodiments, the capture antibody or antigen-binding fragment is an anti-eribulin antibody or antigen-binding fragment as disclosed herein. In some embodiments, the capture antibody or antigen-binding fragment is 5E4. In some embodiments, the 5E4 is an antigen-binding fragment. In some embodiments, the 5E4 is a Fab fragment. In some embodiments, the 5E4 is biotinylated. In some embodiments, the 5E4 is immobilized on a solid support. In some embodiments, the detection antibody or antigen-binding fragment is an anti-ID antibody or antigen-binding fragment. In some embodiments, the anti-ID antibody or antigen-binding fragment is conjugated to a detectable label. In some embodiments, the detectable label is a fluorescent tag. In some embodiments, the detection antibody or antigen-binding fragment is an anti-human IgG Fc antibody or antigen-binding fragment. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment binds the CH2 domain. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment is conjugated to a detectable label. In some embodiments, the detectable label is a fluorescent tag.

[00305] In some embodiments, the DAR insensitive assay quantifies an intact anti-HER2 ADC. In some embodiments, the capture antibody or antigen-binding fragment is an anti-eribulin antibody or antigen-binding fragment as disclosed herein. In some embodiments, the capture antibody or antigen-binding fragment is 5E4. In some embodiments, the 5E4 is an antigen-binding fragment. In some embodiments, the 5E4 is a Fab fragment. In some embodiments, the 5E4 is biotinylated. In some embodiments, the 5E4 is immobilized on a solid support. In some embodiments, the detection antibody or antigen-binding fragment is an anti-ID antibody or antigen-binding fragment. In some embodiments, the anti-ID antibody or antigen-binding fragment is conjugated to a detectable label. Anti-ID trastuzumab antibodies are known in the art and include, e.g., FAB95471R (R&D Systems). In some embodiments, the detectable label is a fluorescent tag. In some embodiments, the detection antibody or antigen-binding fragment is an anti-human IgG Fc antibody or antigen-binding fragment. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment binds the CH2 domain. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment is conjugated to a detectable label. In some embodiments, the detectable label is a fluorescent tag.

[00306] In various embodiments, the assay is DAR sensitive. In some embodiments, a capture antibody or antigen-binding fragment in a DAR sensitive assay is an anti-ID antibody or antigen-binding fragment. In some embodiments, an anti-ID antibody or antigen-binding fragment is the target antigen (e.g., FRA, MSLN, HER2) of the antibody to be captured. In some embodiments, a capture antibody or antigen-binding fragment is an anti-human IgG Fc antibody or antigen-binding fragment. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment binds the CH2 domain. In some embodiments, the capture antibody or antigen-binding fragment is an antigen-binding fragment. In some embodiments, the capture antigen-binding fragment is a Fab fragment. In some embodiments, the capture antibody or antigen-binding fragment is biotinylated. In some embodiments, the capture antibody or antigen-binding fragment is immobilized on a solid support. In some embodiments, the detection antibody or antigen-binding fragment is an anti-eribulin antibody or antigen-binding fragment as disclosed herein. In some embodiments, the capture antibody or antigen-binding fragment is 5E4. In some embodiments, the 5E4 is an antigen-binding fragment. In some embodiments, the 5E4 is a Fab fragment. In some embodiments, the 5E4 is conjugated to a detectable label. In some embodiments, the detectable label is a fluorescent tag.

[00307] In some embodiments, a method for detecting intact ADC in a DAR sensitive manner is provided herein. In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered an ADC. In some embodiments, the method further comprises contacting the biological sample with an anti-ID antibody or antigen-binding fragment or with an anti-human IgG Fc antibody or antigen-binding fragment. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment binds the CH2 domain. In some embodiments, the anti-ID antibody or antigen-binding fragment and/or the anti-human IgG Fc antibody or antigen-binding fragment is biotinylated. In some embodiments, the anti-ID antibody or antigen-binding fragment and/or the anti-human IgG Fc antibody or antigen-binding fragment is immobilized on a solid support. In some embodiments, the method further comprises contacting the biological sample with 5E4. In some embodiments, the 5E4 is a Fab fragment. In some embodiments, the 5E4 is conjugated to a detectable label, e.g., a fluorescent tag. In some embodiments, a signal from the detectable label is detected for quantification of the intact ADC. In some embodiments, the anti-ID antibody is 2G9 or an antigen-binding fragment thereof. In some

embodiments, the anti-ID antibody is an anti-345A12 idiotypic antibody or antigen-binding fragment thereof. In some embodiments, the intact ADC is MORAb-202. In some embodiments, the intact MORAb-202 has DAR4. In some embodiments, the intact ADC is MORAb-109. In some embodiments, the intact MORAb-109 has DAR2. In some embodiments, the intact MORAb-109 has DAR4.

[00308] In some embodiments, the DAR sensitive assay quantifies an intact anti-FRA ADC. In some embodiments, the capture antibody or antigen-binding fragment is an anti-ID antibody or antigen-binding fragment. In some embodiments, the anti-ID antibody or antigen-binding fragment is 2G9. In some embodiments, the 2G9 is an antigen-binding fragment. In some embodiments, the 2G9 is a Fab fragment. In some embodiments, the 2G9 is biotinylated. In some embodiments, the 2G9 is immobilized on a solid support. In some embodiments, the capture antibody or antigen-binding fragment is an anti-human IgG Fc antibody or antigen-binding fragment. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment binds the CH2 domain. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment is biotinylated. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment is immobilized on a solid support. In some embodiments, the detection antibody or antigen-binding fragment is an anti-eribulin antibody or antigen-binding fragment as disclosed herein. In some embodiments, the anti-eribulin antibody or antigen-binding fragment is 5E4. In some embodiments, the 5E4 is an antigen-binding fragment. In some embodiments, the 5E4 is a Fab fragment. In some embodiments, the 5E4 is conjugated to a detectable label. In some embodiments, the detectable label is a fluorescent tag.

[00309] In some embodiments, the DAR sensitive assay quantifies an intact anti-MSLN ADC. In some embodiments, the capture antibody or antigen-binding fragment is an anti-ID antibody or antigen-binding fragment. In some embodiments, the anti-ID antibody or antigen-binding fragment is an antigen-binding fragment. In some embodiments, the anti-ID antibody or antigen-binding fragment is a Fab fragment. In some embodiments, the anti-ID antibody or antigen-binding fragment is biotinylated. In some embodiments, the anti-ID antibody or antigen-binding fragment is immobilized on a solid support. In some embodiments, the capture antibody or antigen-binding fragment is an anti-human IgG Fc antibody or antigen-binding fragment. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment binds the CH2 domain. In some embodiments, the anti-human IgG Fc antibody or

antigen-binding fragment is biotinylated. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment is immobilized on a solid support. In some embodiments, the detection antibody or antigen-binding fragment is an anti-eribulin antibody or antigen-binding fragment as disclosed herein. In some embodiments, the anti-eribulin antibody or antigen-binding fragment is 5E4. In some embodiments, the 5E4 is an antigen-binding fragment. In some embodiments, the 5E4 is a Fab fragment. In some embodiments, the 5E4 is conjugated to a detectable label. In some embodiments, the detectable label is a fluorescent tag.

[00310] In some embodiments, the DAR sensitive assay quantifies an intact anti-HER2 ADC. In some embodiments, the capture antibody or antigen-binding fragment is an anti-ID antibody or antigen-binding fragment. In some embodiments, the anti-ID antibody or antigen-binding fragment is an antigen-binding fragment. In some embodiments, the anti-ID antibody or antigen-binding fragment is a Fab fragment. In some embodiments, the anti-ID antibody or antigen-binding fragment is biotinylated. In some embodiments, the anti-ID antibody or antigen-binding fragment is immobilized on a solid support. In some embodiments, the capture antibody or antigen-binding fragment is an anti-human IgG Fc antibody or antigen-binding fragment. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment binds the CH2 domain. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment is biotinylated. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment is immobilized on a solid support. In some embodiments, the detection antibody or antigen-binding fragment is an anti-eribulin antibody or antigen-binding fragment as disclosed herein. In some embodiments, the anti-eribulin antibody or antigen-binding fragment is 5E4. In some embodiments, the 5E4 is an antigen-binding fragment. In some embodiments, the 5E4 is a Fab fragment. In some embodiments, the 5E4 is conjugated to a detectable label. In some embodiments, the detectable label is a fluorescent tag.

Quantifying Linker-Payload

[00311] In some embodiments, a method for detecting a metabolite of an ADC comprises an assay to quantify free linker-payload, i.e., linker-payload not conjugated to an antibody. In some embodiments, linker-payload is quantified in a biological sample. In some embodiments, the biological sample is plasma. In some embodiments, the assay comprises

immunodepletion. In some embodiments, the assay does not comprise immunodepletion. In some embodiments, the assay comprises a sandwich immunoassay. An exemplary method disclosed herein quantifies linker-payload by immunodepletion of ADC and/or unconjugated antibody or antigen-binding fragment followed by fluorescent detection of linker-payload using a sandwich immunoassay.

[00312] In various embodiments, the immunodepletion step of the assay comprises contacting the sample with a first antibody (“immunodepletion antibody”) or antigen-binding fragment capable of specifically binding to an antibody portion of an antibody-drug conjugate and/or an unconjugated antibody or antigen-binding fragment in the biological sample. In some embodiments, the immunodepletion antibody or antigen-binding fragment is conjugated to a solid support. In some embodiments, the immunodepletion antibody or antigen-binding fragment is conjugated to a label. In some embodiments, the label is a bead, e.g., an agarose bead or a magnetic bead. In some embodiments, bead is a magnetic bead. In some embodiments, the antibody portion of an antibody-drug conjugate and/or an unconjugated antibody or antigen-binding fragment bound to the immunodepletion antibody are immunodepleted from the biological sample. In some embodiments, the immunodepletion is performed by centrifugation, e.g., using agarose bead-labeled immunodepletion antibody or antigen-binding fragment. In some embodiments, the immunodepletion is performed by magnetic separation, e.g., using magnetic bead-labeled immunodepletion antibody or antigen-binding fragment.

[00313] In some embodiments, the immunodepletion antibody or antigen-binding fragment specifically binds an ADC comprising an anti-FRA antibody or antigen-binding fragment thereof. In some embodiments, the ADC is MORAb-202. In some embodiments, the ADC comprises farletuzumab or an antigen-binding fragment thereof. In some embodiments, the ADC comprises an antibody comprising three heavy chain CDRs and three light chain CDRs as follows: HCDR1 comprising SEQ ID NO: 49, HCDR2 comprising SEQ ID NO: 50, HCDR3 comprising SEQ ID NO: 51; LCDR1 comprising SEQ ID NO: 52, LCDR2 comprising SEQ ID NO: 53, and LCDR3 comprising SEQ ID NO: 54, as defined by the Kabat numbering system. In some embodiments, the ADC comprises an antibody comprising three heavy chain CDRs and three light chain CDRs as follows: HCDR1 comprising SEQ ID NO: 55, HCDR2 comprising SEQ ID NO: 56, HCDR3 comprising SEQ ID NO: 57; LCDR1 comprising SEQ ID NO: 58, LCDR2 comprising SEQ ID NO: 59, and LCDR3 comprising

SEQ ID NO: 60, as defined by the IMGT numbering system. In some embodiments, the ADC comprises an antibody comprising a heavy chain variable domain comprising a sequence of SEQ ID NO: 61 and a light chain variable domain comprising a sequence of SEQ ID NO: 62. In some embodiments, the ADC comprises an antibody comprising a heavy chain of SEQ ID NO: 63 and a light chain sequence of SEQ ID NO: 64.

[00314] In some embodiments, the immunodepletion antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment binds the CH2 domain. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment is conjugated to a label. In some embodiments, the label is a bead, e.g., an agarose bead or a magnetic bead. In some embodiments, bead is a magnetic bead.

[00315] In some embodiments, the immunodepletion antibody or antigen-binding fragment comprises an anti-FRA idiotypic antibody or antigen-binding fragment. In some embodiments, the anti-idiotypic antibody or antigen-binding fragment comprises an anti-farletuzumab antibody or antigen-binding fragment as disclosed herein. In some embodiments, the anti-farletuzumab antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 1 (HCDR1), SEQ ID NO: 2 (HCDR2), and SEQ ID NO: 3 (HCDR3); and three LCDRs comprising SEQ ID NO: 4 (LCDR1), SEQ ID NO: 5 (LCDR2), and SEQ ID NO: 6 (LCDR3) as defined by the Kabat numbering system. In some embodiments, an anti-farletuzumab antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 7 (HCDR1), SEQ ID NO: 8 (HCDR2), and SEQ ID NO: 9 (HCDR3); and three LCDRs comprising SEQ ID NO: 10 (LCDR1), SEQ ID NO: 11 (LCDR2), and SEQ ID NO: 12 (LCDR3), as defined by the IMGT numbering system.

[00316] In some embodiments, the anti-farletuzumab antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 13 and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 14.

[00317] In some embodiments, the anti-farletuzumab antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 15 and a light chain comprising an amino acid sequence of SEQ ID NO: 16.

[00318] In some embodiments, the anti-farletuzumab antibody or antigen-binding fragment is antibody 2G9.

[00319] In some embodiments, the anti-farletuzumab antibody or antigen-binding fragment is conjugated to a label. In some embodiments, the label is a bead, e.g., an agarose bead or a magnetic bead. In some embodiments, bead is a magnetic bead.

[00320] In some embodiments, the immunodepletion antibody or antigen-binding fragment specifically binds an ADC comprising an anti-MSLN antibody or antigen-binding fragment thereof. In some embodiments, the ADC is MORAb-109. In some embodiments, the ADC comprises 345A12 or an antigen-binding fragment thereof. In some embodiments, the ADC comprises an antibody comprising three heavy chain CDRs and three light chain CDRs as follows: HCDR1 comprising SEQ ID NO: 65, HCDR2 comprising SEQ ID NO: 66, HCDR3 comprising SEQ ID NO: 67; LCDR1 comprising SEQ ID NO: 68, LCDR2 comprising SEQ ID NO: 69, and LCDR3 comprising SEQ ID NO: 70, as defined by the Kabat numbering system. In some embodiments, the ADC comprises an antibody comprising three heavy chain CDRs and three light chain CDRs as follows: HCDR1 comprising SEQ ID NO: 71, HCDR2 comprising SEQ ID NO: 72, HCDR3 comprising SEQ ID NO: 73; LCDR1 comprising SEQ ID NO: 74, LCDR2 comprising SEQ ID NO: 75, and LCDR3 comprising SEQ ID NO: 76, as defined by the IMGT numbering system. In some embodiments, the ADC comprises an antibody comprising a heavy chain variable domain comprising a sequence of SEQ ID NO: 77 and a light chain variable domain comprising a sequence of SEQ ID NO: 78. In some embodiments, the ADC comprises an antibody comprising a heavy chain of SEQ ID NO: 79 and a light chain sequence of SEQ ID NO: 80.

[00321] In some embodiments, the immunodepletion antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment binds the CH2 domain. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment is conjugated to a label. In some embodiments, the label is a bead, e.g., an agarose bead or a magnetic bead. In some embodiments, bead is a magnetic bead.

[00322] In some embodiments, the immunodepletion antibody or antigen-binding fragment comprises an anti-345A12 idiotypic antibody or antigen-binding fragment. In some embodiments, the anti-idiotypic antibody or antigen-binding fragment comprises an anti-345A12 idiotypic antibody or antigen-binding fragment as disclosed herein. In some embodiments, the anti-345A12 idiotypic antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 273 (HCDR1), SEQ ID NO:

274 (HCDR2), and SEQ ID NO: 275 (HCDR3); and three LCDRs comprising SEQ ID NO: 276 (LCDR1), SEQ ID NO: 277 (LCDR2), and SEQ ID NO: 278 (LCDR3) as defined by the Kabat numbering system. In some embodiments, an anti-345A12 idiotypic antibody or antigen-binding fragment comprises three HCDRs comprising amino acid sequences of SEQ ID NO: 279 (HCDR1), SEQ ID NO: 280 (HCDR2), and SEQ ID NO: 281 (HCDR3); and three LCDRs comprising SEQ ID NO: 282 (LCDR1), SEQ ID NO: 283 (LCDR2), and SEQ ID NO: 284 (LCDR3), as defined by the IMGT numbering system.

[00323] In some embodiments, the anti-345A12 idiotypic antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285 and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286.

[00324] In some embodiments, the anti-345A12 idiotypic antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 287 and a light chain comprising an amino acid sequence of SEQ ID NO: 288.

[00325] In some embodiments, the anti-345A12 idiotypic antibody or antigen-binding fragment is antibody M000053.

[00326] In some embodiments, the anti-345A12 antibody or antigen-binding fragment is conjugated to a label. In some embodiments, the label is a bead, e.g., an agarose bead or a magnetic bead. In some embodiments, bead is a magnetic bead.

[00327] In some embodiments, the immunodepletion antibody or antigen-binding fragment specifically binds an ADC comprising HER2 or an antigen-binding fragment thereof. In some embodiments, the ADC comprises trastuzumab or an antigen-binding fragment thereof. In some embodiments, the ADC comprises an antibody comprising three heavy chain CDRs and three light chain CDRs as follows: HCDR1 comprising SEQ ID NO: 254, HCDR2 comprising SEQ ID NO: 255, HCDR3 comprising SEQ ID NO: 256; LCDR1 comprising SEQ ID NO: 257, LCDR2 comprising SEQ ID NO: 258, and LCDR3 comprising SEQ ID NO: 259, as defined by the Kabat numbering system. In some embodiments, the ADC comprises an antibody comprising three heavy chain CDRs and three light chain CDRs as follows: HCDR1 comprising SEQ ID NO: 260, HCDR2 comprising SEQ ID NO: 261, HCDR3 comprising SEQ ID NO: 262; LCDR1 comprising SEQ ID NO: 263, LCDR2 comprising SEQ ID NO: 264, and LCDR3 comprising SEQ ID NO: 265, as defined by the IMGT numbering system. In some embodiments, the ADC comprises an antibody comprising

a heavy chain variable domain comprising a sequence of SEQ ID NO: 266 and a light chain variable domain comprising a sequence of SEQ ID NO: 267. In some embodiments, the ADC comprises an antibody comprising a heavy chain of SEQ ID NO: 268 and a light chain sequence of SEQ ID NO: 269.

[00328] In some embodiments, the immunodepletion antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment binds the CH2 domain. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment is conjugated to a label. In some embodiments, the label is a bead, e.g., an agarose bead or a magnetic bead. In some embodiments, bead is a magnetic bead.

[00329] In some embodiments, the immunodepletion antibody or antigen-binding fragment comprises an anti-trastuzumab idiotypic antibody or antigen-binding fragment. Anti-trastuzumab idiotypic antibodies or antigen-binding fragments thereof are known in the art and include, e.g., FAB95471R (R&D Systems).

[00330] In some embodiments, the anti-trastuzumab antibody or antigen-binding fragment is conjugated to a label. In some embodiments, the label is a bead, e.g., an agarose bead or a magnetic bead. In some embodiments, bead is a magnetic bead.

[00331] In some embodiments, the sandwich immunoassay comprises contacting the sample with a second antibody ("capture antibody") or antigen-binding fragment and a third antibody ("detection antibody") or antigen-binding fragment. In some embodiments, the capture antibody or antigen-binding fragment is biotinylated. In some embodiments, the capture antibody or antigen-binding fragment is immobilized on a solid support. In some embodiments, the detection antibody or antigen-binding fragment is immobilized on a solid support. In some embodiments, the detection antibody or antigen-binding fragment is conjugated to a detectable label. In some embodiments, the detectable label is a fluorescent label. In some embodiments, the assay comprises detecting a signal from the detectable label on the detection antibody. In some embodiments, the linker-payload in the biological sample is quantified using the signal from the detectable label.

[00332] In some embodiments, the capture antibody or antigen-binding fragment is an anti-eribulin antibody or antigen-binding fragment as disclosed herein. In some embodiments, the capture antibody or antigen-binding fragment is 5E4. In some embodiments, the capture antibody or antigen-binding fragment is an anti-VCP antibody or antigen-binding fragment as

provided herein. In some embodiments, the anti-VCP antibody is antibody 11G6. In some embodiments, the capture antibody or antigen-binding fragment is an antigen-binding fragment. In some embodiments, the capture antibody or antigen-binding fragment is a Fab fragment. In some embodiments, the capture antibody or antigen-binding fragment is biotinylated. In some embodiments, the capture antibody or antigen-binding fragment is immobilized on a solid support.

[00333] In some embodiments, the detection antibody or antigen-binding fragment is an anti-VCP antibody or antigen-binding fragment as provided herein. In some embodiments, the anti-VCP antibody is 11G6. In some embodiments, the detection antibody or antigen-binding fragment is an anti-eribulin antibody or antigen-binding fragment as disclosed herein. In some embodiments, the detection antibody or antigen-binding fragment is 5E4. In some embodiments, the detection antibody or antigen-binding fragment is an antigen-binding fragment. In some embodiments, the detection antibody or antigen-binding fragment is a Fab fragment. In some embodiments, the detection antibody or antigen-binding fragment is conjugated to a detectable label. In some embodiments, the detectable label is a fluorescent tag.

[00334] In some embodiments, the capture antibody or antigen-binding fragment is 5E4. In some embodiments, 5E4 is an antigen-binding fragment. In some embodiments, 5E4 is a Fab fragment. In some embodiments, 5E4 is biotinylated. In some embodiments, 5E4 is immobilized on a solid support. In some embodiments, the the detection antibody or antigen-binding fragment is 11G6. In some embodiments, 11G6 is conjugated to a detectable label. In some embodiments, the detectable label is a fluorescent tag.

[00335] In some embodiments, the limit of quantification of the linker-payload (e.g., VCP-eribulin) in plasma is at least 1.0 ng/mL, at least 1.5 ng/mL, at least 2.0 ng/mL, at least 2.5 ng/mL, at least 3.0 ng/mL, at least 3.5 ng/mL, at least 4.0 ng/mL, at least 4.5 ng/mL, or at least 5.0 ng/mL as measured by Gyrolab xPand immunoassay.

[00336] In some embodiments, the detection antibody or antigen-binding fragment is an anti-albumin antibody or antigen-binding fragment. Anti-albumin antibodies are well known in the art. Any species-specific anti-albumin antibody known in the art may be used in the assays disclosed herein. Albumin is an abundant circulating protein found in plasma. The presence of an unpaired cysteine on albumin provides a possible conjugation site for free linker-payload in circulation. To accurately quantitate linker-payload metabolites in

circulation, it may therefore be important to detect albumin-linker-payload conjugates in addition to free linker-payload conjugates.

[00337] In some embodiments, a linker-payload metabolite in circulation may react with an albumin protein to produce an albumin-linker-payload conjugate. In some embodiments, the albumin-linker-payload conjugate comprises albumin-VCP-eribulin. In some embodiments, the albumin-linker-payload conjugate comprises albumin-Mal-(PEG)_m-VCP-eribulin. In some embodiments, the albumin-linker-payload conjugate comprises albumin-Mal-(PEG)₂-VCP-eribulin.

[00338] In some embodiments, the anti-albumin antibody or antigen-binding fragment is conjugated to a detectable label. In some embodiments, the detectable label is a fluorescent tag.

[00339] In various embodiments, a method for detecting a linker-payload metabolite of MORAb-202 is provided herein. In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered MORAb-202. In some embodiments, the method further comprises contacting the biological sample with antibody 2G9. In some embodiments, the 2G9 is conjugated to a magnetic bead. In some embodiments, contacting the biological sample with antibody 2G9 immunodepletes the MORAb-202 or an antibody or antigen-binding fragment thereof. In some embodiments, the method further comprises contacting the biological sample with antibody 5E4. In some embodiments, the 5E4 is biotinylated and immobilized on a solid support. In some embodiments, the method further comprises contacting the biological sample with antibody 11G6. In some embodiments, the 11G6 is conjugated to a detectable label, e.g., a fluorescent tag. In some embodiments, a signal from the detectable label is detected for quantification of the linker-payload metabolite. In some embodiments, the linker-payload metabolite comprises VCP-eribulin. In some embodiments, the linker-payload metabolite comprises Mal-(PEG)₂-VCP-eribulin.

[00340] In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered MORAb-202. In some embodiments, the method further comprises contacting the biological sample with antibody 2G9. In some embodiments, the 2G9 is conjugated to a magnetic bead. In some embodiments, contacting the biological sample with antibody 2G9 immunodepletes the MORAb-202 or an antibody or antigen-binding fragment thereof. In some embodiments, the method further comprises contacting the

biological sample with antibody 5E4. In some embodiments, the 5E4 is biotinylated and immobilized on a solid support. In some embodiments, the method further comprises contacting the biological sample with an anti-albumin antibody. In some embodiments, the anti-albumin antibody is conjugated to a detectable label, e.g., a fluorescent tag. In some embodiments, a signal from the detectable label is detected for quantification of the linker-payload metabolite. In some embodiments, the linker-payload metabolite comprises VCP-eribulin. In some embodiments, the linker-payload metabolite comprises Mal-(PEG)₂-VCP-eribulin.

[00341] In various other embodiments, a method for detecting a linker-payload metabolite of MORAb-109 is provided herein. In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered MORAb-109. In some embodiments, the method further comprises contacting the biological sample with an anti-human IgG Fc antibody or antigen-binding fragment. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment binds the CH2 domain. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment is conjugated to a magnetic bead. In some embodiments, contacting the biological sample with the anti-human IgG Fc antibody or antigen-binding fragment immunodepletes the MORAb-109 or an antibody or antigen-binding fragment thereof. In some embodiments, the method further comprises contacting the biological sample with antibody 5E4. In some embodiments, the 5E4 is biotinylated and immobilized on a solid support. In some embodiments, the method further comprises contacting the biological sample with antibody 11G6. In some embodiments, the 11G6 is conjugated to a detectable label, e.g., a fluorescent tag. In some embodiments, a signal from the detectable label is detected for quantification of the linker-payload metabolite. In some embodiments, the linker-payload metabolite comprises VCP-eribulin. In some embodiments, the linker-payload metabolite comprises Mal-(PEG)₂-VCP-eribulin.

[00342] In some embodiments, the method comprises obtaining a biological sample from a subject who has been administered MORAb-109. In some embodiments, the method further comprises contacting the biological sample with an anti-human IgG Fc antibody or antigen-binding fragment. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment binds the CH2 domain. In some embodiments, the anti-human IgG Fc antibody or antigen-binding fragment is conjugated to a magnetic bead. In some embodiments, contacting the biological sample with antibody anti-human IgG Fc antibody or antigen-binding fragment

immunodepletes the MORAb-109 or an antibody or antigen-binding fragment thereof. In some embodiments, the method further comprises contacting the biological sample with antibody 5E4. In some embodiments, the 5E4 is biotinylated and immobilized on a solid support. In some embodiments, the method further comprises contacting the biological sample with an anti-albumin antibody. In some embodiments, the anti-albumin antibody is conjugated to a detectable label, e.g., a fluorescent tag. In some embodiments, a signal from the detectable label is detected for quantification of the linker-payload metabolite. In some embodiments, the linker-payload metabolite comprises VCP-eribulin. In some embodiments, the linker-payload metabolite comprises Mal-(PEG)₂-VCP-eribulin.

[00343] In various embodiments, the method disclosed herein may also be used to detect a linker-payload metabolite of an anti-HER2 ADC.

[00344] In various embodiments, kits are provided, which may comprise the antibodies disclosed herein and one or more other containers associated therewith that comprise materials desirable from a commercial and user standpoint, including buffers, diluents, filters, needles, syringes; carrier, package, container, vial and/or tube labels listing contents and/or instructions for use, and package inserts with instructions for use.

[00345] A label may be present on or with the kit to indicate that the kit is used for a specific therapy or non-therapeutic application, such as a prognostic, prophylactic, diagnostic, or laboratory application. A label may also indicate directions for either *in vivo* or *in vitro* use, such as those described herein. Directions and or other information may also be included on an insert(s) or label(s), which is included with or on the kit. The label may be on or associated with the container. A label may be on a container when letters, numbers, or other characters forming the label are molded or etched into the container itself. A label may be associated with a kit when it is present within a receptacle or carrier that also holds the container, e.g., as a package insert.

[00346] It will be readily apparent to those skilled in the art that other suitable modifications and adaptations of the methods of the invention described herein are obvious and may be made using suitable equivalents without departing from the scope of the invention or the embodiments disclosed herein. Having now described the invention in detail, the same will be more clearly understood by reference to the following examples, which are included for purposes of illustration only and are not intended to be limiting.

EXEMPLARY EMBODIMENTS

1. A method for detecting a metabolite of an antibody-drug conjugate, wherein the metabolite is a linker-payload and the payload moiety is eribulin, the method comprising:
 - a) obtaining a biological sample from a subject who has been administered the antibody-drug conjugate;
 - b) contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the antibody-drug conjugate and/or an unconjugated antibody or antigen-binding fragment;
 - c) contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to the payload moiety of the linker-payload;
 - d) contacting the biological sample with a third antibody or antigen-binding fragment, wherein the third antibody or antigen-binding fragment is capable of specifically binding to the linker of the linker-payload; and
 - e) detecting a signal from the third antibody or antigen-binding fragment, thereby detecting the metabolite in the biological sample.

2. A method for detecting a metabolite of an antibody-drug conjugate, wherein the metabolite is a linker-payload and the payload moiety is eribulin, the method comprising:
 - a) obtaining a biological sample from a subject who has been administered the antibody-drug conjugate;
 - b) contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the antibody-drug conjugate and/or an unconjugated antibody or antigen-binding fragment;
 - c) contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to the payload moiety of the linker-payload;
 - d) contacting the biological sample with a third antibody or antigen-binding fragment, wherein the third antibody or antigen-binding fragment is capable of specifically binding to albumin; and
 - e) detecting a signal from the third antibody or antigen-binding fragment, thereby detecting the metabolite in the biological sample.

3. The method of embodiment 1 or embodiment 2, wherein the contacting of the biological sample with the first antibody immunodepletes intact antibody-drug conjugate from the biological sample.
4. The method of any one of embodiments 1 to 3, wherein the first, second, and/or third antibody or antigen-binding fragment is conjugated to a detectable label, a biotin, or a bead.
5. The method of embodiment 4, wherein the first antibody or antigen-binding fragment is conjugated to a biotin.
6. The method of embodiment 4, wherein the first antibody or antigen-binding fragment is conjugated to a bead, preferably a magnetic bead.
7. The method of any one of embodiments 4 to 6, wherein the second antibody or antigen-binding fragment is conjugated to a biotin.
8. The method of embodiment 5 or embodiment 7, wherein the first and/or second antibody or antigen-binding fragment is immobilized on a solid support.
9. The method of any one of embodiments 4 to 8, wherein the third antibody or antigen-binding fragment is conjugated to a detectable label.
10. The method of embodiment 9, wherein the detectable label is a fluorescent tag.
11. The method of any one of embodiments 4 to 10, wherein detecting the metabolite comprises detecting a signal from the detectable label on the third antibody or antigen-binding fragment.
12. The method of any one of embodiments 1 to 11, further comprising quantifying the amount of linker-payload in the biological sample by detecting a signal from the detectable label on the third antibody or antigen-binding fragment.

13. The method of embodiment 12, wherein the signal from the detectable label on the third antibody or antigen-binding fragment comprises a fluorescent signal.
14. The method of any one of embodiments 1 to 13, wherein the antibody-drug conjugate comprises an anti-folate receptor alpha (FRA) antibody or antigen-binding fragment, and/or wherein the unconjugated antibody or antigen-binding fragment is an anti-FRA antibody or a fragment thereof.
15. The method of embodiment 14, wherein the antibody-drug conjugate comprises farletuzumab or an antigen-binding fragment thereof, and/or wherein the unconjugated antibody or antigen-binding fragment is farletuzumab or a fragment thereof.
16. The method of any one of embodiments 1 to 15, wherein the first antibody or antigen-binding fragment specifically binds an anti-FRA antibody or antigen-binding fragment thereof.
17. The method of any one of embodiments 1 to 16, wherein the first antibody or antigen-binding fragment specifically binds farletuzumab or a fragment thereof.
18. The method of embodiment 17, wherein the first antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 13, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 14.
19. The method of embodiment 17, wherein the first antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 1 (HCDR1), SEQ ID NO: 2 (HCDR2), and SEQ ID NO: 3 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 4 (LCDR1), SEQ ID NO: 5 (LCDR2), and SEQ ID NO: 6 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 7

(HCDR1), SEQ ID NO: 8 (HCDR2), and SEQ ID NO: 9 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 10 (LCDR1), SEQ ID NO: 11 (LCDR2), and SEQ ID NO: 12 (LCDR3), as defined by the IMGT numbering system.

20. The method of any one of embodiments 16 to 19, wherein the first antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 13, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 14.

21. The method of any one of embodiments 16 to 19, wherein the first antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 15, and a light chain comprising an amino acid sequence of SEQ ID NO: 16.

22. The method of any one of embodiments 16 to 21, wherein the first antibody is 2G9.

23. The method of any one of embodiments 1 to 13, wherein the antibody-drug conjugate comprises an anti-mesothelin (MSLN) antibody or antigen-binding fragment, and/or wherein the unconjugated antibody or antigen-binding fragment is an anti-MSLN antibody or a fragment thereof.

24. The method of embodiment 23, wherein the antibody-drug conjugate comprises 345A12-HC15-LC4 or an antigen-binding fragment thereof, and/or wherein the unconjugated antibody or antigen-binding fragment is 345A12-HC15-LC4 or a fragment thereof.

25. The method of any one of embodiments 1 to 13, 23, or 24, wherein the first antibody or antigen-binding fragment specifically binds an anti-MSLN antibody or antigen-binding fragment.

26. The method of any one of embodiments 1 to 13 or 23 to 25, wherein the first antibody or antigen-binding fragment specifically binds 345A12-HC15-LC4 or a fragment thereof.

27. The method of embodiment 26, wherein the first antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286.

28. The method of embodiment 26, wherein the first antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 273 (HCDR1), SEQ ID NO: 274 (HCDR2), and SEQ ID NO: 275 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 276 (LCDR1), SEQ ID NO: 277 (LCDR2), and SEQ ID NO: 278 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 279 (HCDR1), SEQ ID NO: 280 (HCDR2), and SEQ ID NO: 281 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 282 (LCDR1), SEQ ID NO: 283 (LCDR2), and SEQ ID NO: 284 (LCDR3), as defined by the IMGT numbering system.

29. The method of any one of embodiments 25 to 28, wherein the first antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286.

30. The method of any one of embodiments 25 to 29, wherein the first antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 287, and a light chain comprising an amino acid sequence of SEQ ID NO: 288.

31. The method of any one of embodiments 1 to 13, wherein the first antibody or antigen-binding fragment is an anti-human IgG Fc antibody or antigen-binding fragment thereof.

32. The method of any one of embodiments 1 to 31, wherein the second antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions

from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 29, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 30.

33. The method of any one of embodiments 1 to 32, wherein the second antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 17 (HCDR1), SEQ ID NO: 18 (HCDR2), and SEQ ID NO: 19 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 20 (LCDR1), SEQ ID NO: 21 (LCDR2), and SEQ ID NO: 22 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 23 (HCDR1), SEQ ID NO: 24 (HCDR2), and SEQ ID NO: 25 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 26 (LCDR1), SEQ ID NO: 27 (LCDR2), and SEQ ID NO: 28 (LCDR3), as defined by the IMGT numbering system.

34. The method of embodiment 32 or embodiment 33, wherein the second antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 29, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 30.

35. The method of any one of embodiments 32 to 34, wherein the second antibody or antigen-binding fragment is an antigen-binding fragment, preferably a Fab fragment.

36. The method of any one of embodiments 32 to 35, wherein the second antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 31 or SEQ ID NO: 294, and a light chain comprising an amino acid sequence of SEQ ID NO: 32.

37. The method of any one of embodiments 32 to 36, wherein the second antibody or antigen-binding fragment is 5E4.

38. The method of any one of embodiments 1 to 37, wherein the second antibody or antigen-binding fragment binds to eribulin with a binding affinity of at least 0.9 nM, at least 1.0 nM, at least 1.1 nM, or at least 1.2 nM.
39. The method of any one of embodiments 1 to 38, wherein the linker-payload comprises Val-Cit-pAb-eribulin ("VCP-eribulin").
40. The method of embodiment 39, wherein the linker-payload comprises Mal-(PEG)₂-VCP-eribulin.
41. The method of any one of embodiments 1 to 40, wherein the linker-payload comprises Mal-(PEG)₂-VCP-eribulin, wherein the Mal moiety is conjugated to albumin.
42. The method of any one of embodiments 1 or 3 to 41, wherein the third antibody or antigen-binding fragment specifically binds Val-Cit-pAB ("VCP").
43. The method of embodiment 42, wherein the third antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 45, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 46.
44. The method of embodiment 42 or embodiment 43, wherein the third antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 33 (HCDR1), SEQ ID NO: 34 (HCDR2), and SEQ ID NO: 35 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 36 (LCDR1), SEQ ID NO: 37 (LCDR2), and SEQ ID NO: 38 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 39 (HCDR1), SEQ ID NO: 40 (HCDR2), and SEQ ID NO: 41 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID

NO: 42 (LCDR1), SEQ ID NO: 43 (LCDR2), and SEQ ID NO: 38 (LCDR3), as defined by the IMGT numbering system.

45. The method of any one of embodiments 42 to 44, wherein the third antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 45, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 46.

46. The method of any one of embodiments 42 to 45, wherein the third antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 47, and a light chain comprising an amino acid sequence of SEQ ID NO: 48.

47. The method of any one of embodiments 42 to 46, wherein the third antibody or antigen-binding fragment is 11G6.

48. The method of any one of embodiments 1 to 47, wherein the biological sample comprises whole blood, plasma, and/or serum from a patient.

49. The method of any one of embodiments 4 to 48, wherein the detectable label comprises a fluorescent tag, a luminescent tag, an electrochemiluminescent tag, or an enzyme reporter.

50. The method of embodiment 49, wherein the detectable label is a fluorescent tag, a luminescent tag, or an electrochemiluminescent tag.

51. The method of any one of embodiments 1 to 50, wherein the first antibody or antigen-binding fragment is conjugated to a magnetic bead, the second antibody or antigen-binding fragment is conjugated to a biotin, and the third antibody or antigen-binding fragment is conjugated to a fluorescent tag.

52. The method of any one of embodiments 1 or 3 to 51, wherein the linker-payload comprises VCP-eribulin, and wherein the limit of quantification of the VCP-eribulin is at

least 1.0 ng/mL, at least 1.5 ng/mL, at least 2.0 ng/mL, at least 2.5 ng/mL, at least 3.0 ng/mL, at least 3.5 ng/mL, at least 4.0 ng/mL, at least 4.5 ng/mL, or at least 5.0 ng/mL as measured by Gyrolab xPand immunoassay, wherein the biological sample comprises plasma.

53. The method of any one of embodiments 1 to 52, wherein the limit of quantification for the eribulin is at least 5 pg/mL, at least 10 pg/mL, at least 15 pg/mL, or at least 20 pg/mL as measured by multiple reaction monitoring (MRM) detection.

54. The method of any one of embodiments 1 to 53, wherein the limit of quantification for eribulin is at least 10 pg/mL as measured by multiple reaction monitoring (MRM) detection.

55. A method for detecting a metabolite of an antibody-drug conjugate, wherein the metabolite is a linker-payload comprising Val-Cit-pAB-eribulin ("VCP-eribulin") and the payload moiety is eribulin, wherein the antibody-drug conjugate is MORAb-202, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-202;
 - b) contacting the biological sample with 2G9;
 - c) contacting the biological sample with 5E4;
 - d) contacting the biological sample with 11G6; and
 - e) detecting a signal from 11G6,
- thereby detecting the metabolite in the biological sample.

56. A method for detecting a metabolite of an antibody-drug conjugate, wherein the metabolite is a linker-payload comprising Val-Cit-pAB-eribulin ("VCP-eribulin") and the payload moiety is eribulin, wherein the antibody-drug conjugate is MORAb-202, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-202;
- b) contacting the biological sample with 2G9;
- c) contacting the biological sample with 5E4;

- d) contacting the biological sample with an anti-albumin antibody; and
- e) detecting a signal from the anti-albumin antibody,
thereby detecting the metabolite in the biological sample.

57. The method of embodiment 55 or embodiment 56, wherein the contacting of the biological sample with the 2G9 immunodepletes intact MORAb-202 from the biological sample.

58. The method of any one of embodiments 55 to 57, wherein the 2G9 is conjugated to a biotin or a magnetic bead.

59. The method of any one of embodiments 55 to 58, wherein the 5E4 is conjugated to a biotin.

60. The method of embodiment 59, wherein the 5E4 is immobilized on a solid support.

61. The method of any one of embodiments 55 to 60, wherein the 11G6 or anti-albumin antibody is conjugated to a detectable label, preferably wherein the detectable label is a fluorescent tag.

62. The method of embodiment 61, wherein detecting the metabolite comprises detecting a signal from the detectable label.

63. The method of embodiment 61 or embodiment 62, further comprising quantifying the amount of VCP-eribulin in the biological sample by detecting a signal from the detectable label.

64. A method for detecting a metabolite of an antibody-drug conjugate, wherein the metabolite is a linker-payload comprising Val-Cit-pAB-eribulin ("VCP-eribulin") and the payload moiety is eribulin, wherein the antibody-drug conjugate is MORAb-109, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-109;
- b) contacting the biological sample with a first antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment comprises an anti-human IgG Fc or an anti-idiotypic antibody or antigen binding fragment, wherein the anti-idiotypic antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286;
- c) contacting the biological sample with 5E4;
- d) contacting the biological sample with 11G6; and
- e) detecting a signal from 11G6,
thereby detecting the metabolite in the biological sample.

65. A method for detecting a metabolite of an antibody-drug conjugate, wherein the metabolite is a linker-payload comprising Val-Cit-pAB-eribulin ("VCP-eribulin") and the payload moiety is eribulin, wherein the antibody-drug conjugate is MORAb-109, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-109;
- b) contacting the biological sample with a first antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment comprises an anti-human IgG Fc or an anti-idiotypic antibody or antigen binding fragment, wherein the anti-idiotypic antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286;
- c) contacting the biological sample with 5E4;
- d) contacting the biological sample with an anti-albumin antibody; and
- e) detecting a signal from the anti-albumin antibody,
thereby detecting the metabolite in the biological sample.

66. The method of embodiment 64 or embodiment 65, wherein the contacting of the biological sample with the first antibody or antigen-binding fragment immunodepletes intact MORAb-109 from the biological sample.
67. The method of any one of embodiments 64 to 66, wherein the first antibody or antigen-binding fragment is conjugated to a biotin.
68. The method of any one of embodiments 64 to 66, wherein the first antibody or antigen-binding fragment is conjugated to a bead, preferably a magnetic bead.
69. The method of any one of embodiments 64 to 68, wherein the 5E4 is conjugated to a biotin.
70. The method of embodiment 69, wherein the 5E4 is immobilized on a solid support.
71. The method of any one of embodiments 64 to 70, wherein the 11G6 or the anti-albumin antibody is conjugated to a detectable label, preferably wherein the detectable label is a fluorescent tag.
72. The method of embodiment 71, wherein detecting the metabolite comprises detecting a signal from the detectable label.
73. The method of embodiment 71 or embodiment 72, further comprising quantifying the amount of VCP-eribulin in the biological sample by detecting a signal from the detectable label.
74. The method of any one of embodiments 55 to 73, wherein 5E4 binds to eribulin with a binding affinity of at least 0.9 nM, at least 1.0 nM, at least 1.1 nM, or at least 1.2 nM.
75. A method for detecting total antibody-drug conjugate (ADC) and/or unconjugated antibody or antigen-binding fragment, wherein the ADC is MORAb-202 and the

unconjugated antibody or antigen-binding fragment is farletuzumab or an antigen-binding fragment thereof, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-202;
- b) contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC and/or an unconjugated antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment is an anti-idiotypic antibody, wherein the anti-idiotypic antibody specifically binds farletuzumab or a fragment thereof;
- c) contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to a second epitope of the antibody portion of the ADC and/or the unconjugated antibody or antigen-binding fragment, wherein the second antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment; and
- d) detecting a signal from the second antibody or antigen-binding fragment, thereby detecting the total ADC and/or unconjugated antibody or antigen-binding fragment in the biological sample.

76. A method for detecting total antibody-drug conjugate (ADC) and/or unconjugated antibody or antigen-binding fragment, wherein the ADC is MORAb-202 and the unconjugated antibody or antigen-binding fragment is farletuzumab or an antigen-binding fragment thereof, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-202;
- b) contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC and/or the unconjugated antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment;
- c) contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to a second epitope of the antibody portion of the ADC and/or the unconjugated antibody or antigen-binding fragment, wherein

the second antibody or antigen-binding fragment is an anti-idiotypic antibody, wherein the anti-idiotypic antibody specifically binds farletuzumab or a fragment thereof; and

d) detecting a signal from the second antibody or antigen-binding fragment, thereby detecting the total ADC and/or unconjugated antibody or antigen-binding fragment in the biological sample.

77. The method of embodiment 75 or embodiment 76, wherein the anti-idiotypic antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 13, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 14.

78. The method of embodiment 75 or embodiment 76, wherein the anti-idiotypic antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 1 (HCDR1), SEQ ID NO: 2 (HCDR2), and SEQ ID NO: 3 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 4 (LCDR1), SEQ ID NO: 5 (LCDR2), and SEQ ID NO: 6 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 7 (HCDR1), SEQ ID NO: 8 (HCDR2), and SEQ ID NO: 9 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 10 (LCDR1), SEQ ID NO: 11 (LCDR2), and SEQ ID NO: 12 (LCDR3), as defined by the IMGT numbering system.

79. The method of any one of embodiments 75 to 78, wherein the anti-idiotypic antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 13, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 14.

80. The method of any one of embodiments 75 to 79, wherein the anti-idiotypic antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 15, and a light chain comprising an amino acid sequence of SEQ ID NO: 16.

81. The method of any one of embodiments 75 to 80, wherein the anti-idiotypic antibody is 2G9.

82. A method for detecting total antibody-drug conjugate (ADC) and/or unconjugated antibody or antigen-binding fragment, wherein the ADC is MORAb-109 and the unconjugated antibody or antigen-binding fragment is 345A12-HC15-LC4 or an antigen-binding fragment thereof, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-109;
- b) contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC and/or the unconjugated antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment is an anti-idiotypic antibody, wherein the anti-idiotypic antibody specifically binds 345A12-HC15-LC4 or a fragment thereof;
- c) contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to a second epitope of the antibody portion of the ADC and/or the unconjugated antibody or antigen-binding fragment, wherein the second antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment; and
- d) detecting a signal from the second antibody or antigen-binding fragment, thereby detecting the total ADC and/or unconjugated antibody or antigen-binding fragment in the biological sample.

83. A method for detecting total antibody-drug conjugate (ADC) and/or unconjugated antibody or antigen-binding fragment, wherein the ADC is MORAb-109 and the unconjugated antibody or antigen-binding fragment is 345A12-HC15-LC4 or an antigen-binding fragment thereof, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-109;
- b) contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC and/or the unconjugated antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment;
- c) contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to a second epitope of the antibody portion of the ADC and/or the unconjugated antibody or antigen-binding fragment, wherein the second antibody or antigen-binding fragment is an anti-idiotypic antibody, wherein the anti-idiotypic antibody specifically binds 345A12-HC15-LC4 or a fragment thereof; and
- d) detecting a signal from the second antibody or antigen-binding fragment, thereby detecting the total ADC and/or antibody or antigen-binding fragment in the biological sample.

84. The method of embodiment 82 or embodiment 83, wherein the anti-idiotypic antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286.

85. The method of embodiment 82 or embodiment 83, wherein the anti-idiotypic antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 273 (HCDR1), SEQ ID NO: 274 (HCDR2), and SEQ ID NO: 275 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 276 (LCDR1), SEQ ID NO: 277 (LCDR2), and SEQ ID NO: 278 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 279 (HCDR1), SEQ ID NO: 280 (HCDR2), and SEQ ID NO: 281 (HCDR3); and three light chain complementarity determining regions comprising amino acid

sequences of SEQ ID NO: 282 (LCDRI), SEQ ID NO: 283 (LCDR2), and SEQ ID NO: 284 (LCDR3), as defined by the IMGT numbering system.

86. The method of any one of embodiments 83 to 85, wherein the anti-idiotypic antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286.

87. The method of any one of embodiments 83 to 86, wherein the anti-idiotypic antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 287, and a light chain comprising an amino acid sequence of SEQ ID NO: 288.

88. A method for detecting total antibody-drug conjugate (ADC) and/or unconjugated antibody or antigen-binding fragment, wherein the ADC is MORAb-202 and the unconjugated antibody or antigen-binding fragment is farletuzumab or an antigen-binding fragment thereof, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-202;
- b) contacting the biological sample with a first antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment comprises 2G9;
- c) contacting the biological sample with a second antibody or antigen-binding fragment, wherein the second antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment; and
- d) detecting a signal from second antibody or antigen-binding fragment, thereby detecting the total ADC and/or unconjugated antibody or antigen-binding fragment in the biological sample.

89. A method for detecting total antibody-drug conjugate (ADC) and/or unconjugated antibody or antigen-binding fragment, wherein the ADC is MORAb-202 and the unconjugated antibody or antigen-binding fragment is farletuzumab or an antigen-binding fragment thereof, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-202;

- b) contacting the biological sample with a first antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment;
- c) contacting the biological sample with a second antibody or antigen-binding fragment, wherein the second antibody or antigen-binding fragment comprises 2G9; and
- d) detecting a signal from the second antibody or antigen-binding fragment, thereby detecting the total ADC and/or unconjugated antibody or antigen-binding fragment in the biological sample.

90. A method for detecting total antibody-drug conjugate (ADC) and/or unconjugated antibody or antigen-binding fragment, wherein the ADC is MORAb-109 and the unconjugated antibody or antigen-binding fragment is 345A12-HC15-LC4 or an antigen-binding fragment thereof, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-109;
- b) contacting the biological sample with a first antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286;
- c) contacting the biological sample with a second antibody or antigen-binding fragment, wherein the second antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment; and
- d) detecting a signal from second antibody or antigen-binding fragment, thereby detecting the total ADC and/or antibody or unconjugated antigen-binding fragment in the biological sample.

91. A method for detecting total antibody-drug conjugate (ADC) and/or unconjugated antibody or antigen-binding fragment, wherein the ADC is MORAb-109 and the unconjugated antibody or antigen-binding fragment is 345A12-HC15-LC4 or an antigen-binding fragment thereof, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-109;

- b) contacting the biological sample with a first antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment;
 - c) contacting the biological sample with a second antibody or antigen-binding fragment, wherein the second antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286; and
 - d) detecting a signal from the second antibody or antigen-binding fragment, thereby detecting the total ADC and/or unconjugated antibody or antigen-binding fragment in the biological sample.
92. The method of any one of embodiments 75 to 91, wherein the first antibody or antigen-binding fragment is conjugated to a biotin or a bead, preferably a biotin.
93. The method of embodiment 92, wherein the first antibody or antigen-binding fragment is immobilized on a solid support.
94. The method of any one of embodiments 75 to 93, wherein the second antibody or antigen-binding fragment is conjugated to a detectable label.
95. The method of embodiment 94, wherein the detectable label is a fluorescent tag.
96. The method of any one of embodiments 75 to 95, wherein the first antibody or antigen-binding fragment is conjugated to a biotin, and the second antibody or antigen-binding fragment is conjugated to a fluorescent tag.
97. The method of any one of embodiments 75 to 96, wherein detecting the total ADC and/or unconjugated antibody or antigen-binding fragment comprises detecting a signal from the detectable label.

98. The method of any one of embodiments 75 to 97, further comprising quantifying the amount of total ADC and/or unconjugated antibody or antigen-binding fragment in the biological sample by detecting a signal from the detectable label.
99. The method of any one of embodiments 75 to 98, wherein the biological sample comprises whole blood, plasma, and/or serum from a patient.
100. A method for detecting intact antibody-drug conjugate (ADC), wherein the ADC is MORAb-202, the method comprising:
- a) obtaining a biological sample from a subject who has been administered MORAb-202;
 - b) contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to eribulin;
 - c) contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC, wherein the second antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment or an anti-idiotypic antibody or antigen-binding fragment, wherein the anti-idiotypic antibody specifically binds farletuzumab or a fragment thereof; and
 - d) detecting a signal from the second antibody or antigen-binding fragment, thereby detecting the intact ADC in the biological sample.
101. A method for detecting intact antibody-drug conjugate (ADC), wherein the ADC is MORAb-202, the method comprising:
- a) obtaining a biological sample from a subject who has been administered MORAb-202;
 - b) contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC and/or an antigen-binding fragment thereof, wherein the first antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment or an anti-idiotypic antibody or antigen-binding fragment, wherein the anti-idiotypic antibody specifically binds farletuzumab or a fragment thereof;

- c) contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to eribulin; and
- d) detecting a signal from the second antibody or antigen-binding fragment, thereby detecting the intact ADC in the biological sample.

102. The method of embodiment 100 or embodiment 101, wherein the anti-idiotypic antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 13, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 14.

103. The method of embodiment 100 or embodiment 101, wherein the anti-idiotypic antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 1 (HCDR1), SEQ ID NO: 2 (HCDR2), and SEQ ID NO: 3 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 4 (LCDR1), SEQ ID NO: 5 (LCDR2), and SEQ ID NO: 6 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 7 (HCDR1), SEQ ID NO: 8 (HCDR2), and SEQ ID NO: 9 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 10 (LCDR1), SEQ ID NO: 11 (LCDR2), and SEQ ID NO: 12 (LCDR3), as defined by the IMGT numbering system.

104. The method of any one of embodiments 100 to 103, wherein the anti-idiotypic antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 13, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 14.

105. The method of any one of embodiments 100 to 104, wherein the anti-idiotypic antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 15, and a light chain comprising an amino acid sequence of SEQ ID NO: 16.

106. The method of any one of embodiments 100 to 105, wherein the anti-idiotypic antibody is 2G9.

107. A method for detecting intact antibody-drug conjugate (ADC), wherein the ADC is MORAb-109, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-109;
- b) contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to eribulin;
- c) contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC, wherein the second antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment or an anti-idiotypic antibody or antigen-binding fragment, wherein the anti-idiotypic antibody specifically binds 345A12-HC15-LC4 or a fragment thereof; and
- d) detecting a signal from the second antibody or antigen-binding fragment, thereby detecting the intact ADC in the biological sample.

108. A method for detecting intact antibody-drug conjugate (ADC), wherein the ADC is MORAb-109, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-109;
- b) contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC, wherein the first antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment or an anti-idiotypic antibody or antigen-binding fragment, wherein the anti-idiotypic antibody specifically binds 345A12-HC15-LC4 or a fragment thereof;
- c) contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to eribulin; and
- d) detecting a signal from the second antibody or antigen-binding fragment,

thereby detecting the intact ADC in the biological sample.

109. The method of embodiment 107 or embodiment 108, wherein the anti-idiotypic antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286.

110. The method of embodiment 107 or embodiment 108, wherein the anti-idiotypic antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 273 (HCDR1), SEQ ID NO: 274 (HCDR2), and SEQ ID NO: 275 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 276 (LCDR1), SEQ ID NO: 277 (LCDR2), and SEQ ID NO: 278 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 279 (HCDR1), SEQ ID NO: 280 (HCDR2), and SEQ ID NO: 281 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 282 (LCDR1), SEQ ID NO: 283 (LCDR2), and SEQ ID NO: 284 (LCDR3), as defined by the IMGT numbering system.

111. The method of any one of embodiments 107 to 110, wherein the anti-idiotypic antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286.

112. The method of any one of embodiments 107 to 111, wherein the anti-idiotypic antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 287, and a light chain comprising an amino acid sequence of SEQ ID NO: 288.

113. The method of any one of embodiments 100 to 112, wherein the first and/or second antibody or antigen-binding fragment capable of specifically binding to eribulin is an antigen-binding fragment, preferably a Fab fragment.

114. The method of any one of embodiments 100 to 113, wherein the first and/or second antibody or antigen-binding fragment capable of specifically binding to eribulin comprises three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 29, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 30.

115. The method of any one of embodiments 100 to 113, wherein the first and/or second antibody or antigen-binding fragment capable of specifically binding to eribulin comprises three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 17 (HCDR1), SEQ ID NO: 18 (HCDR2), and SEQ ID NO: 19 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 20 (LCDR1), SEQ ID NO: 21 (LCDR2), and SEQ ID NO: 22 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 23 (HCDR1), SEQ ID NO: 24 (HCDR2), and SEQ ID NO: 25 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 26 (LCDR1), SEQ ID NO: 27 (LCDR2), and SEQ ID NO: 28 (LCDR3), as defined by the IMGT numbering system.

116. The method of any one of embodiments 100 to 115, wherein the first and/or second antibody or antigen-binding fragment capable of specifically binding to eribulin comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 29, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 30.

117. The method of any one of embodiments 100 to 116, wherein the first and/or second antibody or antigen-binding fragment capable of specifically binding to eribulin comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 31 or SEQ ID NO: 294, and a light chain comprising an amino acid sequence of SEQ ID NO: 32.

118. The method of any one of embodiments 100 to 117, wherein the first and/or second antibody or antigen-binding fragment capable of specifically binding to eribulin is 5E4.

119. The method of any one of embodiments 100 to 118, wherein the first and/or second antibody or antigen-binding fragment capable of specifically binding to eribulin binds to eribulin with a binding affinity of at least 0.9 nM, at least 1.0 nM, at least 1.1 nM, or at least 1.2 nM.

120. A method for detecting intact antibody-drug conjugate (ADC), wherein the ADC is MORAb-202, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-202;
- b) contacting the biological sample with a first antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment is 5E4;
- c) contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC, wherein the second antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment or is 2G9 or an antigen-binding fragment thereof; and
- d) detecting a signal from the second antibody or antigen-binding fragment, thereby detecting the intact ADC in the biological sample.

121. A method for detecting intact antibody-drug conjugate (ADC), wherein the ADC is MORAb-202, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-202;
- b) contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC and/or an antigen-binding fragment thereof, wherein the first antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment, or is 2G9 or an antigen-binding fragment;

- c) contacting the biological sample with a second antibody or antigen-binding, wherein the second antibody or antigen-binding fragment is 5E4; and
- d) detecting a signal from the second antibody or antigen-binding fragment, thereby detecting the intact ADC in the biological sample.

122. A method for detecting intact antibody-drug conjugate (ADC), wherein the ADC is MORAb-109, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-109;
- b) contacting the biological sample with a first antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment is 5E4;
- c) contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC, wherein the second antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment or an anti-idiotypic antibody or antigen-binding fragment, wherein the anti-idiotypic antibody comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286; and
- d) detecting a signal from the second antibody or antigen-binding fragment, thereby detecting the intact ADC in the biological sample.

123. A method for detecting intact antibody-drug conjugate (ADC), wherein the ADC is MORAb-109, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-109;
- b) contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC and/or an antigen-binding fragment thereof, wherein the first antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment, or an anti-idiotypic antibody or antigen binding fragment, wherein the anti-idiotypic antibody or antigen-binding fragment comprises a heavy chain variable region

comprising an amino acid sequence of SEQ ID NO: 285, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286;

- c) contacting the biological sample with a second antibody or antigen-binding, wherein the second antibody or antigen-binding fragment is 5E4; and
- d) detecting a signal from the second antibody or antigen-binding fragment, thereby detecting the intact ADC in the biological sample.

124. The method of any one of embodiments 100 to 123, wherein the first antibody or antigen-binding fragment is conjugated to a biotin or a bead, preferably a biotin.

125. The method of embodiment 124, wherein the first antibody or antigen-binding fragment is immobilized on a solid support.

126. The method of any one of embodiments 100 to 125, wherein the second antibody or antigen-binding fragment is conjugated to a detectable label.

127. The method of embodiment 126, wherein the detectable label is a fluorescent tag.

128. The method of any one of embodiments 100 to 127, wherein the first antibody or antigen-binding fragment is conjugated to a biotin, and the second antibody or antigen-binding fragment is conjugated to a fluorescent tag.

129. The method of any one of embodiments 100 to 128, wherein detecting the intact ADC comprises detecting a signal from the detectable label.

130. The method of any one of embodiments 100 to 129, further comprising quantifying the amount of intact ADC in the biological sample by detecting a signal from the detectable label.

131. The method of any one of embodiments 100 to 130, wherein the biological sample comprises whole blood, plasma, and/or serum from a patient.

132. A method for detecting intact and/or total antibody-drug conjugate (ADC) and/or a metabolite of an ADC, wherein the metabolite is unconjugated antibody or antigen-binding fragment, linker-payload, and/or free payload, comprising two or more of:

- a) the method of any one of embodiments 1 to 74;
- b) the method of any one of embodiments 75 to 99;
- c) the method of any one of embodiments 100, 102 to 107, 109 to 120, 122, 124 to

132;

- d) the method of any one of embodiments 101 to 106, 108 to 119, 121, 123 to 132;

and

e) a method comprising quantification of free payload, wherein the free payload is eribulin, wherein the eribulin is quantified by multiple reaction monitoring.

133. An antibody or antigen-binding fragment thereof capable of binding to an antibody-drug conjugate comprising farletuzumab and/or to farletuzumab or an antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 13, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 14.

134. The antibody or antigen-binding fragment of embodiment 133, wherein the antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 1 (HCDR1), SEQ ID NO: 2 (HCDR2), and SEQ ID NO: 3 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 4 (LCDR1), SEQ ID NO: 5 (LCDR2), and SEQ ID NO: 6 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 7 (HCDR1), SEQ ID NO: 8 (HCDR2), and SEQ ID NO: 9 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 10 (LCDR1), SEQ ID NO: 11 (LCDR2), and SEQ ID NO: 12 (LCDR3), as defined by the IMGT numbering system.

135. The antibody or antigen-binding fragment of embodiment 133 or embodiment 134, wherein the antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 13, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 14.

136. The antibody or antigen-binding fragment of any one of embodiments 133 to 134, wherein the antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 15, and a light chain comprising an amino acid sequence of SEQ ID NO: 16.

137. The antibody or antigen-binding fragment of any one of embodiments 133 to 136, wherein the antibody or antigen-binding fragment is conjugated to a label.

138. The antibody or antigen-binding fragment of embodiment 137, wherein the label comprises a fluorescent tag, an enzyme reporter, a biotin, or a bead.

139. The antibody or antigen-binding fragment of embodiment 138, wherein the label is a biotin.

140. The antibody or antigen-binding fragment of embodiment 138, wherein the label is a bead, optionally an agarose bead or a magnetic bead.

141. The antibody or antigen-binding fragment of embodiment 138, wherein the label is a fluorescent tag.

142. An antibody or antigen-binding fragment that binds the same epitope as or competes for binding with 2G9.

143. An antibody or antigen-binding fragment thereof capable of binding to an antibody-drug conjugate comprising 345A12-HC15-LC4 and/or to 345A12-HC15-LC4 or an antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions from a heavy chain variable region

comprising an amino acid sequence of SEQ ID NO: 285, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286.

144. The antibody or antigen-binding fragment of embodiment 143, wherein the antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 273 (HCDR1), SEQ ID NO: 274 (HCDR2), and SEQ ID NO: 275 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 276 (LCDR1), SEQ ID NO: 277 (LCDR2), and SEQ ID NO: 278 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 279 (HCDR1), SEQ ID NO: 280 (HCDR2), and SEQ ID NO: 281 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 282 (LCDR1), SEQ ID NO: 283 (LCDR2), and SEQ ID NO: 284 (LCDR3), as defined by the IMGT numbering system.

145. The antibody or antigen-binding fragment of embodiment 143 or embodiment 144, wherein the antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286.

146. The antibody or antigen-binding fragment of any one of embodiments 143 to 145, wherein the antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 287, and a light chain comprising an amino acid sequence of SEQ ID NO: 288.

147. The antibody or antigen-binding fragment of any one of embodiments 143 to 146, wherein the antibody or antigen-binding fragment is conjugated to a label.

148. The antibody or antigen-binding fragment of embodiment 147, wherein the label comprises a fluorescent tag, an enzyme reporter, a biotin, or a bead.

149. The antibody or antigen-binding fragment of embodiment 148, wherein the label is a biotin.

150. The antibody or antigen-binding fragment of embodiment 148, wherein the label is a bead, optionally an agarose bead or a magnetic bead.

151. The antibody or antigen-binding fragment of embodiment 148, wherein the label is a fluorescent tag.

152. An antibody or antigen-binding fragment thereof capable of binding to eribulin, wherein the antibody or antigen-binding fragment comprises

(i) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 29, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 30;

(ii) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 101, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 102;

(iii) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 119, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 120;

(iv) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 137, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 138;

(v) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 153, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 154;

(vi) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 169, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 170;

(vii) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 183, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 184;

(viii) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 200, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 201;

(ix) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 217, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 218; or

(x) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 234, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 235.

153. The antibody or antigen-binding fragment thereof of embodiment 152, wherein the antibody or antigen-binding fragment comprises

(i) three heavy chain complementarity determining regions (HCDRs) comprising amino acid sequences of SEQ ID NO: 17 (HCDR1), SEQ ID NO: 18 (HCDR2), and SEQ ID NO: 19 (HCDR3); and three light chain complementarity determining regions (LCDRs) comprising amino acid sequences of SEQ ID NO: 20 (LCDR1), SEQ ID NO: 21 (LCDR2), and SEQ ID NO: 22 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 23 (HCDR1), SEQ ID NO: 24 (HCDR2), and SEQ ID NO: 25 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID

NO: 26 (LCDR1), SEQ ID NO: 27 (LCDR2), and SEQ ID NO: 28 (LCDR3), as defined by the IMGT numbering system;

(ii) three HCDRs comprising amino acid sequences of SEQ ID NO: 89 (HCDR1), SEQ ID NO: 90 (HCDR2), and SEQ ID NO: 91 (HCDR3); and three LCDRs comprising SEQ ID NO: 92 (LCDR1), SEQ ID NO: 93 (LCDR2), and SEQ ID NO: 94 (LCDR3) as defined by the Kabat numbering system; or three HCDRs comprising amino acid sequences of SEQ ID NO: 95 (HCDR1), SEQ ID NO: 96 (HCDR2), and SEQ ID NO: 97 (HCDR3); and three LCDRs comprising SEQ ID NO: 98 (LCDR1), SEQ ID NO: 99 (LCDR2), and SEQ ID NO: 100 (LCDR3) as defined by the IMGT numbering system;

(iii) three HCDRs comprising amino acid sequences of SEQ ID NO: 107 (HCDR1), SEQ ID NO: 108 (HCDR2), and SEQ ID NO: 109 (HCDR3); and three LCDRs comprising SEQ ID NO: 110 (LCDR1), SEQ ID NO: 111 (LCDR2), and SEQ ID NO: 112 (LCDR3) as defined by the Kabat numbering system; or three HCDRs comprising amino acid sequences of SEQ ID NO: 113 (HCDR1), SEQ ID NO: 114 (HCDR2), and SEQ ID NO: 115 (HCDR3); and three LCDRs comprising SEQ ID NO: 116 (LCDR1), SEQ ID NO: 117 (LCDR2), and SEQ ID NO: 118 (LCDR3) as defined by the IMGT numbering system;

(iv) three HCDRs comprising amino acid sequences of SEQ ID NO: 125 (HCDR1), SEQ ID NO: 126 (HCDR2), and SEQ ID NO: 127 (HCDR3); and three LCDRs comprising SEQ ID NO: 128 (LCDR1), SEQ ID NO: 129 (LCDR2), and SEQ ID NO: 130 (LCDR3) as defined by the Kabat numbering system; or three HCDRs comprising amino acid sequences of SEQ ID NO: 131 (HCDR1), SEQ ID NO: 132 (HCDR2), and SEQ ID NO: 133 (HCDR3); and three LCDRs comprising SEQ ID NO: 134 (LCDR1), SEQ ID NO: 135 (LCDR2), and SEQ ID NO: 136 (LCDR3) as defined by the IMGT numbering system;

(v) three HCDRs comprising amino acid sequences of SEQ ID NO: 143 (HCDR1), SEQ ID NO: 144 (HCDR2), and SEQ ID NO: 145 (HCDR3); and three LCDRs comprising SEQ ID NO: 146 (LCDR1), SEQ ID NO: 129 (LCDR2), and SEQ ID NO: 147 (LCDR3) as defined by the Kabat numbering system; or three HCDRs comprising amino acid sequences of SEQ ID NO: 148 (HCDR1), SEQ ID NO: 149 (HCDR2), and SEQ ID NO: 150 (HCDR3); and three LCDRs comprising SEQ ID NO: 151 (LCDR1), SEQ ID NO: 135 (LCDR2), and SEQ ID NO: 152 (LCDR3) as defined by the IMGT numbering system;

(vi) three HCDRs comprising amino acid sequences of SEQ ID NO: 159 (HCDR1), SEQ ID NO: 160 (HCDR2), and SEQ ID NO: 161 (HCDR3); and three LCDRs

comprising SEQ ID NO: 162 (LCDR1), SEQ ID NO: 21 (LCDR2), and SEQ ID NO: 163 (LCDR3) as defined by the Kabat numbering system; or three HCDRs comprising amino acid sequences of SEQ ID NO: 164 (HCDR1), SEQ ID NO: 165 (HCDR2), and SEQ ID NO: 166 (HCDR3); and three LCDRs comprising SEQ ID NO: 167 (LCDR1), SEQ ID NO: 27 (LCDR2), and SEQ ID NO: 168 (LCDR3) as defined by the IMGT numbering system;

(vii) three HCDRs comprising amino acid sequences of SEQ ID NO: 175 (HCDR1), SEQ ID NO: 176 (HCDR2), and SEQ ID NO: 109 (HCDR3); and three LCDRs comprising SEQ ID NO: 177 (LCDR1), SEQ ID NO: 111 (LCDR2), and SEQ ID NO: 178 (LCDR3) as defined by the Kabat numbering system; or three HCDRs comprising amino acid sequences of SEQ ID NO: 179 (HCDR1), SEQ ID NO: 180 (HCDR2), and SEQ ID NO: 115 (HCDR3); and three LCDRs comprising SEQ ID NO: 181 (LCDR1), SEQ ID NO: 117 (LCDR2), and SEQ ID NO: 182 (LCDR3) as defined by the IMGT numbering system;

(viii) three HCDRs comprising amino acid sequences of SEQ ID NO: 189 (HCDR1), SEQ ID NO: 190 (HCDR2), and SEQ ID NO: 191 (HCDR3); and three LCDRs comprising SEQ ID NO: 192 (LCDR1), SEQ ID NO: 193 (LCDR2), and SEQ ID NO: 194 (LCDR3) as defined by the Kabat numbering system; or three HCDRs comprising amino acid sequences of SEQ ID NO: 195 (HCDR1), SEQ ID NO: 196 (HCDR2), and SEQ ID NO: 197 (HCDR3); and three LCDRs comprising SEQ ID NO: 198 (LCDR1), SEQ ID NO: 117 (LCDR2), and SEQ ID NO: 199 (LCDR3) as defined by the IMGT numbering system;

(ix) three HCDRs comprising amino acid sequences of SEQ ID NO: 206 (HCDR1), SEQ ID NO: 207 (HCDR2), and SEQ ID NO: 208 (HCDR3); and three LCDRs comprising SEQ ID NO: 44 (LCDR1), SEQ ID NO: 209 (LCDR2), and SEQ ID NO: 210 (LCDR3) as defined by the Kabat numbering system; or three HCDRs comprising amino acid sequences of SEQ ID NO: 211 (HCDR1), SEQ ID NO: 212 (HCDR2), and SEQ ID NO: 213 (HCDR3); and three LCDRs comprising SEQ ID NO: 214 (LCDR1), SEQ ID NO: 215 (LCDR2), and SEQ ID NO: 216 (LCDR3) as defined by the IMGT numbering system; or

(x) three HCDRs comprising amino acid sequences of SEQ ID NO: 223 (HCDR1), SEQ ID NO: 224 (HCDR2), and SEQ ID NO: 225 (HCDR3); and three LCDRs comprising SEQ ID NO: 226 (LCDR1), SEQ ID NO: 227 (LCDR2), and SEQ ID NO: 228 (LCDR3) as defined by the Kabat numbering system; or three HCDRs comprising amino acid sequences of SEQ ID NO: 229 (HCDR1), SEQ ID NO: 230 (HCDR2), and SEQ ID NO: 231

(HCDR3); and three LCDRs comprising SEQ ID NO: 232 (LCDR1), SEQ ID NO: 99 (LCDR2), and SEQ ID NO: 233 (LCDR3) as defined by the IMGT numbering system.

154. The antibody or antigen-binding fragment thereof of embodiment 152 or embodiment 153, wherein the antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 17 (HCDR1), SEQ ID NO: 18 (HCDR2), and SEQ ID NO: 19 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 20 (LCDR1), SEQ ID NO: 21 (LCDR2), and SEQ ID NO: 22 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 23 (HCDR1), SEQ ID NO: 24 (HCDR2), and SEQ ID NO: 25 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 26 (LCDR1), SEQ ID NO: 27 (LCDR2), and SEQ ID NO: 28 (LCDR3), as defined by the IMGT numbering system.

155. The antibody or antigen-binding fragment of embodiment 152 or embodiment 153, wherein the antibody or antigen-binding fragment comprises

- (i) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 29, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 30;
- (ii) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 101, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 102;
- (iii) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 119, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 120;
- (iv) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 137, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 138;
- (v) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 153, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 154;

(vi) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 169, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 170;

(vii) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 183, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 184;

(viii) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 200, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 201;

(ix) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 217, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 218; or

(x) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 234, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 235.

156. The antibody or antigen-binding fragment of any one of embodiments 152 to 155, wherein the antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 29, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 30.

157. The antibody or antigen-binding fragment of any one of embodiments 152 to 156, wherein the antibody or antigen-binding fragment is an antigen-binding fragment, preferably a Fab fragment.

158. The antibody or antigen-binding fragment of any one of embodiments 152 to 157, wherein the antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 31, and a light chain comprising an amino acid sequence of SEQ ID NO: 32.

159. The antibody or antigen-binding fragment of any one of embodiments 152 to 157, wherein the antibody or antigen-binding fragment comprises

- (i) a heavy chain comprising an amino acid sequence of SEQ ID NO: 294 and a light chain comprising an amino acid sequence of SEQ ID NO: 32;
- (ii) a heavy chain comprising an amino acid sequence of SEQ ID NO: 103 and a light chain comprising an amino acid sequence of SEQ ID NO: 104;
- (iii) a heavy chain comprising an amino acid sequence of SEQ ID NO: 121 and a light chain comprising an amino acid sequence of SEQ ID NO: 122;
- (iv) a heavy chain comprising an amino acid sequence of SEQ ID NO: 139 and a light chain comprising an amino acid sequence of SEQ ID NO: 140;
- (v) a heavy chain comprising an amino acid sequence of SEQ ID NO: 155 and a light chain comprising an amino acid sequence of SEQ ID NO: 156;
- (vi) a heavy chain comprising an amino acid sequence of SEQ ID NO: 171 and a light chain comprising an amino acid sequence of SEQ ID NO: 172;
- (vii) a heavy chain comprising an amino acid sequence of SEQ ID NO: 185 and a light chain comprising an amino acid sequence of SEQ ID NO: 186;
- (viii) a heavy chain comprising an amino acid sequence of SEQ ID NO: 202 and a light chain comprising an amino acid sequence of SEQ ID NO: 203;
- (ix) a heavy chain comprising an amino acid sequence of SEQ ID NO: 219 and a light chain comprising an amino acid sequence of SEQ ID NO: 220; or
- (x) a heavy chain comprising an amino acid sequence of SEQ ID NO: 236 and a light chain comprising an amino acid sequence of SEQ ID NO: 237.

160. The antibody or antigen-binding fragment of any one of embodiments 152 to 156 or 159, wherein the antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 294, and a light chain comprising an amino acid sequence of SEQ ID NO: 32.

161. The antibody or antigen-binding fragment of any one of embodiments 152 to 160, wherein the antibody or antigen-binding fragment is conjugated to a label.

162. The antibody or antigen-binding fragment of embodiment 161, wherein the label comprises a fluorescent tag, an enzyme reporter, a biotin, or a bead.

163. The antibody or antigen-binding fragment of embodiment 162, wherein the label is a biotin.

164. The antibody or antigen-binding fragment of embodiment 162, wherein the label is a fluorescent tag.

165. An antibody or antigen-binding fragment thereof capable of binding to Val-Cit-pAB ("VCP"), wherein the antibody or antigen-binding fragment comprises

(i) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 45, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 46; or

(ii) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 248, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 249.

166. The antibody or antigen-binding fragment thereof of claim 165, wherein the antibody or antigen-binding fragment comprises

(i) three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 33 (HCDR1), SEQ ID NO: 34 (HCDR2), and SEQ ID NO: 35 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 36 (LCDR1), SEQ ID NO: 37 (LCDR2), and SEQ ID NO: 38 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 39 (HCDR1), SEQ ID NO: 40 (HCDR2), and SEQ ID NO: 41 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 42 (LCDR1), SEQ ID NO: 43 (LCDR2), and SEQ ID NO: 38 (LCDR3), as defined by the IMGT numbering system; or

(ii) three HCDRs comprising amino acid sequences of SEQ ID NO: 159 (HCDR1), SEQ ID NO: 240 (HCDR2), and SEQ ID NO: 241 (HCDR3); and three LCDRs comprising SEQ ID NO: 242 (LCDR1), SEQ ID NO: 209 (LCDR2), and SEQ ID NO: 243

(LCDR3) as defined by the Kabat numbering system; or three HCDRs comprising amino acid sequences of SEQ ID NO: 164 (HCDR1), SEQ ID NO: 244 (HCDR2), and SEQ ID NO: 245 (HCDR3); and three LCDRs comprising SEQ ID NO: 246 (LCDR1), SEQ ID NO: 215 (LCDR2), and SEQ ID NO: 243 (LCDR3) as defined by the IMGT numbering system.

167. The antibody or antigen-binding fragment thereof of embodiment 165 or embodiment 166, wherein the antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 33 (HCDR1), SEQ ID NO: 34 (HCDR2), and SEQ ID NO: 35 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 36 (LCDR1), SEQ ID NO: 37 (LCDR2), and SEQ ID NO: 38 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 39 (HCDR1), SEQ ID NO: 40 (HCDR2), and SEQ ID NO: 41 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 42 (LCDR1), SEQ ID NO: 43 (LCDR2), and SEQ ID NO: 38 (LCDR3), as defined by the IMGT numbering system.

168. The antibody or antigen-binding fragment of embodiment 165 or embodiment 166, wherein the antibody or antigen-binding fragment comprises

(i) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 45, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 46; or

(ii) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 248, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 249.

169. The antibody or antigen-binding fragment of any one of embodiments 165 to 168, wherein the antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 45, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 46.

170. The antibody or antigen-binding fragment of any one of embodiments 165, 166, or 168, wherein the antibody or antigen-binding fragment comprises

- (i) a heavy chain comprising an amino acid sequence of SEQ ID NO: 47, and a light chain comprising an amino acid sequence of SEQ ID NO: 48; or
- (ii) a heavy chain comprising an amino acid sequence of SEQ ID NO: 250, and a light chain comprising an amino acid sequence of SEQ ID NO: 251.

171. The antibody or antigen-binding fragment of any one of embodiments 165 to 170, wherein the antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 47, and a light chain comprising an amino acid sequence of SEQ ID NO: 48.

172. The antibody or antigen-binding fragment of any one of embodiments 165 to 171, wherein the antibody or antigen-binding fragment is conjugated to a label.

173. The antibody or antigen-binding fragment of embodiment 172, wherein the label comprises a fluorescent tag, an enzyme reporter, a biotin, or a bead.

174. The antibody or antigen-binding fragment of embodiment 172 or embodiment 173, wherein the label is a fluorescent tag.

175. A kit comprising one or more of the antibodies or antigen-binding fragments of any one of embodiments 133 to 174, for detecting a metabolite of an antibody-drug conjugate.

EXAMPLES

Example 1: Generation and screening of recombinant anti-Mal-(PEG)₂-VCP-eribulin antibodies

[00347] To generate antibodies specifically to Mal-(PEG)₂-VCP-eribulin, an approach was taken to conjugate Mal-(PEG)₂-VCP-eribulin to two different proteins, one for immunization in rabbits and one for initial screening. Immunizing and screening reagents are shown in FIG. 2. Keyhole-lymphocyte hemocyanin was used as the immunizing conjugated protein, in order

to elicit the greatest immunogenicity. Screening of hits was done using a bovine serum albumin (BSA) conjugate. Titer of final bleed was ~ 75,000 (FIG. 3).

[00348] Spleen cells from immunized rabbits were plated at limiting dilution and culture supernatants screened by ELISA against BSA-(Mal-(PEG)₂-VCP-eribulin). Sixty-eight BSA-(Mal-(PEG)₂-VCP-eribulin)-reactive wells were used for gene-rescue of variable domains by PCR and 50 clones were able to be rescued with complete VH/VL sequences. These were cloned by In-Fusion cloning into mammalian expression vectors and expressed transiently in HEK-293 cells.

[00349] Twelve clones were selected for further screening using biolayer interferometry (BLI) (FIG. 4A). These clones were screened for binding to BSA-(Mal-(PEG)₂-VCP-eribulin) and human serum albumin (HSA)-PEG₄-DBCO-N₃-PEG₄-eribulin in order to discriminate hits that had specificity to eribulin alone or mal-(PEG)₂-VCP-eribulin (Table 28).

Table 28 – BLI screening of initial 12 gene-rescued hits

clone	binding to Mal-(PEG) ₂ - VCP-eribulin	binding to eribulin
1L5	Y	Y
5E4	Y	Y
5E24	Y	Y
5P14	Y	Y
6A12	Y	Y
6K13	Y	Y
6O11	<u>Y</u>	<u>N</u>
8E8	Y	Y
9H3	Y	Y
11G6	<u>Y</u>	<u>N</u>
12L15	<u>N</u>	<u>Y</u>
12M7	Y	Y

Regular text indicates eribulin-specific clones. Bold underlining indicates Mal-(PEG)₂-VCP-eribulin – specific clones. Underlining indicates non-specific/weak binder.

[00350] Results from screening identified nine clones that were specific to eribulin, while two clones (6O11 and 11G6) bound only to VCP-eribulin. 12L15 demonstrated weak binding

only to eribulin and none to VCP-eribulin. BLI binding data is shown in FIG. 4B. Protein sequences for these 12 clones are listed in FIG. 4C. Six clones were selected for further specificity characterization by BLI. Binding was measured to humanized anti-human folate receptor alpha MORAb-003 (reference), MORAb-003 conjugated with maleimido-PEG₂-Val-Cit-pAB-cryptophycin (DAR4), and MORAb-003 conjugated with mal-(PEG)₂-VCP-eribulin (DAR4), also referred to as MORAb-202 (FIG. 4D). The results of this screening are shown in Table 29.

Table 29 - Characterization of binding of six selected leads to MORAb-003-based ADCs

	MORAb-003	MORAb-003 - mal- PEG ₂ -VCP- cryptophycin	MORAb-003 - Mal- (PEG) ₂ -VCP-eribulin
5E4	N	N	Y
5E24	N	N	Y
5P14	N	N	Y
6O11	N	Y	Y
8E8	Y	N	Y
11G6	N	Y	Y

[00351] Results from the screening demonstrated that 5E4, 5E24, and 5P14 had strong binding to MORAb-003-Mal-(PEG)₂-VCP-eribulin, with no background binding to MORAb-003 alone or MORAb-003-Mal-(PEG)₂-VCP-cryptophycin. Both 6O11 and 11G6 bound to both eribulin- and cryptophycin – conjugated MORAb-003, indicating specificity to the linker portion (Mal-(PEG)₂-VCP), however, 6O11 did demonstrate some background binding to reference tips, and because 11G6 binding was stronger to the VCP-cryptophycin ADC, indicating better linker specificity, it was selected as the linker-specific clone moving forward. 8E8 demonstrated background binding to MORAb-003 and was not examined further. Binding trace data is included in FIG. 4E.

Linker specificity of 11G6

[00352] The specificity of anti-linker antibody 11G6 was further assessed by BLI. Binding of 11G6 to a number of ADCs prepared with various linker-payload structures was performed

with a reference antibody. The results of this study are shown in Table 30. BLI binding curve data is listed in FIG. 4F.

Table 30 - Binding specificity of 11G6

Linker			Binding of 11G6
Spacer	Cleavage site	Payload	
PEG2	Val-Cit-pAB	eribulin	Y
PEG3	Val-Cit-pAB	eribulin	Y
PEG4	Val-Cit-pAB	eribulin	Y
PEG2	Val-Ala-pAB	eribulin	N
PEG1	Asp	eribulin	N
PEG2	Asp	eribulin	N
PEG3	Asp	eribulin	N
caproyl	Asp	eribulin	N
PEG1	Asn	eribulin	N
PEG2	Asn	eribulin	N
PEG3	Asn	eribulin	N
caproyl	Asn	eribulin	N
PEG2	Val-Lys(Me) ₂ -pAB	eribulin	N
PEG2	Ala-Lys(Me) ₂ -pAB	eribulin	N
PEG2	Ala-Ala-Asn	eribulin	N
PEG2	Ala-Ala-Asn(Me)-Asn	eribulin	N
PEG2	Ala-Phe-Lys-pAB	eribulin	N

pAB – para-aminobenzyl

[00353] The results demonstrate that 11G6 has specificity for the VCP structure, as it bound no other cleavage site structure, including VAP. All PEG spacer lengths were bound by 11G6, indicating flexibility of the spacer group structure in binding. These results, when compared with the binding of 5E4 to Mal-(PEG)₂-Val-Cit-pAB-cryptophycin ADC, indicate that 11G6 binds specifically to the VCP epitope. 5E4 was also shown to bind to ADCs occupied with 11G6 in the BLI experiment, identifying 11G6/5E4 as a possible antibody pair for immunoassays quantitating VCP-eribulin structures.

Binding affinity and DAR sensitivity of 5E4

[00354] Anti-eribulin antibody 5E4 was selected for further analysis and assay formatting studies. To begin evaluation of 5E4 as a capture reagent for intact ADC and to assess binding affinity for eribulin-conjugated ADC, evaluation by surface plasmon resonance (SPR) was performed using a BIAcore T-100 system. In this format, biotinylated 5E4 is captured on a streptavidin-coated biosensor surface. Antibodies and ADCs evaluated were MORAb-202 (MORAb-003 conjugated to an average DAR 4.0 of Mal-(PEG)₂-VCP-eribulin), DAR0, DAR2, and DAR4 forms of MORAb-202 purified by preparative-scale hydrophobic interaction chromatography (HIC), and MORAb-202 drug substance (MORAb-003 conjugated to an average DAR 4.0 of Mal-(PEG)₂-VCP-eribulin, prepared under GMP conditions). The isolated DAR forms allow for the assessment of DAR sensitivity of anti-eribulin antibodies as capture agents. The results of this study are shown in Table 31. Sensogram traces with fitting data are shown in FIG. 5. Two anti-eribulin Fab2 reagents, AbD26796 and AbD26798, were included as comparators for 5E4 Fab. These reagents were previously generated in a phage display screen (BioRad); AbD26796 is eribulin-specific, while AbD26798 recognizes VCP-eribulin but not eribulin alone.

Table 31 - Binding assessment of 5E4 by BIAcore to various DAR species of MORAb-202

	MORAb-003	MORAb-202 purified DAR0	MORAb-202 purified DAR2	MORAb-202 purified DAR4	MORAb-202 drug substance
5E4	no binding	1.8 x 10 ⁻⁷	1.2 x 10 ⁻⁹	7.2 x 10 ⁻¹⁰	8.8 x 10 ⁻¹⁰
AbD26796	no binding	no binding	4.0 x 10 ⁻⁸	8.0 x 10 ⁻⁹	8.7 x 10 ⁻⁹
AbD26798	no binding	no binding	1.3 x 10 ⁻⁷	1.8 x 10 ⁻⁸	1.6 x 10 ⁻⁸

Affinity values are in molar (M)

[00355] 5E4 showed nanomolar binding affinity to all conjugated MORAb-003 species. Some residual binding was also seen for the purified DAR0 species, but this is likely due to contaminating DAR1 ADC in the preparation, as 5E4 did not bind to MORAb-003 alone. This affinity (0.9-1.2 nM) was much higher than the other two anti-eribulin reagents evaluated (8.7-40 nM and 16-130 nM). Furthermore, 5E4 Fab demonstrated much less difference between DAR2 and DAR4 species (1.6-fold) than AbD26796 (4.6-fold) and AbD26798 (8.1-fold), indicating ideal properties for use in intact ADC assays.

Example 2: Development and evaluation of anti-eribulin 5E4 in intact ADC assays

[00356] Anti-eribulin 5E4 was evaluated in intact ADC assays for eribulin-conjugated anti-human folate receptor alpha ADC MORAb-202, and for eribulin-conjugated anti-human mesothelin ADC MORAb-202.

MORAb-202 intact ADC assay

[00357] A MORAb-202 intact ADC assay was developed using biotinylated 5E4 monovalent Fab fragment as a capture reagent and an anti-farletuzumab antibody 2G9 as detector on the Gyros XPand platform. Monovalent Fab was used to reduce DAR sensitivity in the assay. A generic format of the assay and binding curve is shown in FIGS. 6A-B.

[00358] The limit of detection in the assay (LOD) in neat human, cynomolgus monkey, rat, and mouse plasma is 27.4 ng/mL. The lower limit of quantitation (LLOQ) in neat human, cynomolgus monkey, rat, and mouse plasma is 27.4 ng/mL. The upper limit of quantitation (ULOQ) in neat human, cynomolgus monkey, rat, and mouse plasma is 20 µg/mL. The minimum required dilution (MRD) of plasma sample is 1:10.

MORAb-109 intact ADC assay

[00359] A MORAb-109 intact ADC was developed using biotinylated 5E4 monovalent Fab fragment as a capture reagent and an anti-human Fc (CH₂-specific) antibody as detector on the Gyros XPand platform. MORAb-109 is an eribulin-conjugated ADC targeting human mesothelin, conjugated with Mal-(PEG)₂-Val-Cit-pAB-eribulin. MORAb-109 DAR₂ form is conjugated at position 80 (cysteine) on the light chain. MORAb-109 DAR₄ form is conjugated at position 80 on the light chain and position 118 on the heavy chain (alanine mutated to cysteine, A118C). A generic format of the assay and binding curve is shown in FIGS. 7A-B.

[00360] The limit of detection in the assay (LOD) in neat human, cynomolgus monkey, rat, and mouse plasma is 141.2 ng/mL. The lower limit of quantitation (LLOQ) in neat human, cynomolgus monkey, rat, and mouse plasma is 141.2 ng/mL. The upper limit of quantitation (ULOQ) in neat human, cynomolgus monkey, rat, and mouse plasma is 16 µg/mL. The minimum required dilution (MRD) of plasma sample is 1:20.

MORAb-109 pharmacokinetics (PK) in normal mice

[00361] This assay was used to measure the PK of MORAb-109 in normal mice. MORAb-109 DAR2 was administered as an IV bolus dose. These results are shown in FIG. 8A. FIG. 8B shows PK data for administration of 25 mg/kg of MORAb-109 and 10 mg/kg MORAb-109 in normal mice. The percent hydrolyzed maleimide and average DAR of MORAb-109 in normal mice is shown in FIG. 8C.

MORAb-109 PK in NCI-H2110 tumor-bearing mice

[00362] The PK of MORAb-109 (DAR2) in NCI-H2110 tumor-bearing mice was measured. Intact ADC and total Ab were measured in both plasma (FIG. 9A) and in tumor lysates (to examine uptake and stability of ADC at the tumor site, compared with plasma) (FIG. 9B) from the mice after treatment with 25 mg/kg or 50 mg/kg MORAb-109. A randomly conjugated form of the ADC (random conjugated at partially-reduced interchain disulfides, followed by isolation of the DAR2 form) was also included, to compare site-specific conjugation with random conjugation. PK parameters in both the plasma and tumor were assessed (FIG. 9C).

MORAb-109 PK in cynomolgus monkeys

[00363] To measure the PK of MORAb-109, mice received an IV bolus administration of 15 mg/kg. Total antibody and intact ADC PK values had similar rates of decline in the concentration of MORAb-109 (FIG. 10A).

[00364] The results of DAR and percent maleimide hydrolysis of MORAb-109 in cynomolgus monkeys exhibited hydrolysis of conjugated maleimide in MORAb-109 stabilizes DAR loss in circulation in monkeys (FIG. 10B).

MORAb-109 PK in normal rats

[00365] The MORAb-109 intact ADC assay was also used to determine PK of DAR2 and DAR4 forms of MORAb-109 in normal rats (FIG. 11A). Further PK results are shown (FIG. 11B).

Trastuzumab ADC: Intact ADC Assay

[00366] A trastuzumab-eribulin intact ADC assay was developed using biotinylated 5E4 monovalent Fab fragment as a capture reagent and an anti-trastuzumab antibody (R&D Systems) as detector on the Gyros XPand platform. This assay was run on trastuzumab conjugated with different eribulin-based linker-payloads. A generic format of the assay and binding curves are shown in FIGS. 12A-B. Because anti-trastuzumab anti-idiotypic antibody was used as a detection antibody, this assay was used not only for wild-type human Fc, but also mutated Fc (1-4-AAS mutant).

[00367] The limit of detection in the assay (LOD) in neat human, cynomolgus monkey, and mouse plasma is 4010 ng/mL. The lower limit of quantitation (LLOQ) in neat human, cynomolgus monkey, and mouse plasma is 4010 ng/mL. The upper limit of quantitation (ULOQ) in neat human, cynomolgus monkey, and mouse plasma is 1 mg/mL. The minimum required dilution (MRD) of plasma sample is 1:100.

[00368] This assay was first applied to measure stability of various trastuzumab-eribulin ADCs in both mouse and human plasma. The ADCs varied in their linker-payload structure. The results are shown in FIG. 13A, including detail of linker-payload structures. Linker-payloads were attached to antibodies via transglutaminase transamidation onto the amide nitrogen of the Gln residue in each linker (indicated in red) (FIG. 13B).

[00369] The assay was next used to measure the levels of a subset of these ADCs described above in mice injected with an IV bolus of the indicated ADC. These results are shown in FIG. 13C. The PK data in mice dosed at either 5 mg/kg or 20 mg/kg is shown in FIG. 13D.

Example 3: Development and use of VCP-eribulin (total unconjugated linker-payload) assay***Linker-payload assay format and dynamic range***

[00370] An assay was developed to measure released linker-payload (VCP-eribulin) from ADCs conjugated with VCP-eribulin-containing linker-payloads. A feature of this assay is efficient immunodepletion of conjugated linker-payload, i.e., intact ADC, from plasma samples. This is done in an antibody-specific manner using either antigen-conjugated magnetic beads (MORAb-109) or anti-idiotypic antibody-conjugated beads (for MORAb-202).

[00371] Free linker-payload is then captured using anti-eribulin 5E4 and detected using the VCP-specific reagent 11G6. The schematic of immunodepletion and detection is shown in FIGS. 14A-B. The limit of detection in the assay (LOD) in neat human, cynomolgus monkey, rat, and mouse plasma is 5 ng/mL. The lower limit of quantitation (LLOQ) in neat human, cynomolgus monkey, rat, and mouse plasma is 5 ng/mL. The upper limit of quantitation (ULOQ) in neat human, cynomolgus monkey, rat, and mouse plasma is 10 µg/mL. The minimum required dilution (MRD) of plasma sample is 1:5000.

Free linker-payload from MORAb-109 DAR2 in mouse plasma

[00372] The linker-payload levels in mouse matrix for MORAb-109 DAR2 were assessed to compare the same antibody conjugated in a random manner with site-specific conjugated DAR2. The linker-payload, and not free payload, was identified as the main metabolite of the ADC (FIG. 15A).

[00373] The DAR shift and percent maleimide hydrolysis of MORAb-109 in mouse plasma was observed over 200 hours (FIG. 15B). Free eribulin and Mal-(PEG)₂-VCP-eribulin from MORAb-109 in mouse plasma was also assessed (FIG. 15C).

Linker-payload from MORAb-109 following maleimide ring opening

[00374] Free linker-payload from MORAb-109 DAR2 was measured following mild-base ring opening of the conjugated maleimide and compared with unmodified MORAb-109 in mouse and human plasma (FIG. 16). The improvement of linker-payload stability following maleimide ring opening and inhibition of retro-Michael release of the linker-payload was demonstrated.

Example 5: Development and use of eribulin-conjugated albumin assays

[00375] Albumin may represent a major form of released linker-payload following retro-Michael release, due to its high concentration in circulation and the presence of an unpaired cysteine that is conserved in evolution. This molecule may represent an active ADC metabolite with a long circulating half-life, and thus may be relevant to quantitate. Using species-specific anti-albumin reagents and the anti-eribulin antibody 5E4, assays were developed to measure eribulin-conjugated albumin in mouse, rat, monkey, and human matrix (FIG. 17).

[00376] Typically, immunodepletion is used to remove the ADC from the sample. While this may not be necessary, without being bound by theory, excess ADC may compete with eribulin-albumin for capture by 5E4 and affect overall assay sensitivity. The limit of detection in the assay (LOD) in neat human, cynomolgus monkey, rat, and mouse plasma is 5 ng/mL. The lower limit of quantitation (LLOQ) in neat human, cynomolgus monkey, rat, and mouse plasma is 5 ng/mL. The upper limit of quantitation (ULOQ) in neat human, cynomolgus monkey, rat, and mouse plasma is 10 µg/mL. The minimum required dilution (MRD) of plasma sample is 1:5000.

MORAb-202 stability in vitro in plasma

[00377] This assay was combined with the total unconjugated linker-payload assay to measure the stability of MORAb-202 in various matrices (FIG. 18A). DAR loss and maleimide hydrolysis were also assessed (FIG. 18B and FIG. 18C).

[00378] When normalized for molarity, these results indicate that albumin conjugate was the main form of eribulin-linker following retro-Michael release of linker-payload, and much more abundant than free payload alone. Levels of linker-payload and eribulin-albumin stabilized after 24 hr in MORAb-202-dosed monkey plasma, presumably due to hydrolysis of the conjugated maleimide ring (FIG. 18D).

Metabolism in MORAb-202-dosed non-Human Primates (NHP)

[00379] Leveraging the anti-eribulin antibody 5E4 and the anti-VCP antibody 11G6 provided a clear picture of the metabolism and fate of MORAb-202 dosed in NHP. Linker-payload and conjugated albumin were measured in plasma samples from cynomolgus monkeys dosed with MORAb-202 at 6 mg/kg or 2 mg/kg (FIG. 19A). PK parameters were also assessed (FIG. 19B).

PK in MORAb-109 doses in normal rats

[00380] Similar to MORAb-202 administered in NHP, MORAb-109 administration in normal rats demonstrated levels of circulating albumin-eribulin conjugate 2-orders of magnitude higher than free eribulin, but much lower than circulating ADC (FIGS. 20A-B). DAR loss due to retro-Michael release was inversely correlated with maleimide hydrolysis (FIG. 20C).

Example 6: Immunohistochemistry using anti-eribulin 5E4

[00381] In addition to its use as a reagent for capturing and quantitating eribulin conjugated species in matrices, 5E4 was also used for immunohistochemical analyses of eribulin-conjugated species in tissues from animals dosed with eribulin-conjugated ADCs. 5E4 antibody was biotinylated prior to staining to allow for detection.

Immunohistochemical (IHC) staining of human ovarian cancer xenograft OVCAR-3 tumors from MORAb-202 – treated mice

[00382] Tumors from OVCAR-3 tumor bearing mice treated with either PBS, eribulin, or MORAb-202 were isolated, fixed and stained with 5E4.

[00383] The results using 5E4 as staining agent show MORAb-202 uptake and retention at the tumor site, while no staining is observed with tumors from PBS- or eribulin-treated mice (FIG. 21). The lack of staining for eribulin in the eribulin-treated mice may be due to eribulin loss during the fixing and washing steps of IHC staining.

IHC staining of human lung cancer xenograft NCI-H2110 tumors from MORAb-109-treated mice (day 3 post-treatment)

[00384] NCI-H2110 human lung cancer xenograft tumors from MORAb-109-treated mice were stained with biotinylated 5E4, along with an anti-human Fc antibody, which will localize human IgG. Serial sections were stained.

[00385] These results, similar to the MORAb-202 study with OVCAR3 tumors, demonstrated uptake of eribulin-conjugated MORAb-109 at the tumor site (FIG. 22). Furthermore, the staining with anti-human Fc on serial section also demonstrates that anti-human IgG colocalizes with anti-eribulin staining, indicating ADC retention.

Example 7: Methods

[00386] The prior examples employed methods that are detailed below.

Methods for isolation of and production of antibodies to Mal-(PEG)₂-VCP-eribulin

[00387] To generate antigen for immunization, bovine serum albumin (BSA) and keyhole-lymphocyte hemocyanin (KLH) were buffer-exchanged into 20 mM sodium phosphate, 150

mM NaCl, 5 mM EDTA, pH 7.5 at final concentrations of 10 mg/mL. Traut's reagent was dissolved in water and added to each at 40x molar excess of Traut's reagent:protein. Reaction was allowed to proceed at room temperature for 1 hr. Unreacted Traut's reagent was removed by centrifugal desalting using Zeba spin desalting columns into the same buffer. Maleimido-PEG₂-valine-citrulline-*para*-aminobenzyl-eribulin (Mal-(PEG)₂-VCP-eribulin) (FIG. 2) was added to each thiolated protein at a molar excess of 6:1 Mal-(PEG)₂-VCP-eribulin:protein for 4 hr at room temperature. Unreacted Mal-(PEG)₂-VCP-eribulin was removed by spin desalting as above. Final conjugation ratio of 2.7:1 and 2.9:1 Mal-(PEG)₂-VCP-eribulin:protein was determined for BSA-(Mal-(PEG)₂-VCP-eribulin) and KLH-(Mal-(PEG)₂-VCP-eribulin), respectively using Elman assay for free thiol content.

Immunization of rabbits and isolation of antigen-positive B-cells

[00388] New Zealand White rabbits (2) were immunized on day 1 with 0.5 mg KLH-(Mal-(PEG)₂-VCP-eribulin) in complete Freund's adjuvant, then again on day 21 and 42 with 0.5 mg KLH-(Mal-(PEG)₂-VCP-eribulin) in Freund's incomplete adjuvant. Evaluation by ELISA on MORAb-202 or BSA-(Mal-(PEG)₂-VCP-eribulin) indicated titers in excess of 1:400,000. Spleens and lymph nodes (pre-scapular, popliteal, and inguinal) were isolated and kept at 4°C. Single cell suspensions were prepared from each and cryopreserved in liquid nitrogen. Irradiated CHO cells expressing RbCD154 were plated at 4,500 cells per well. 24 hours post-plating, B-cells were recovered, treated with DNase I, and stimulated with pokeweed mitogen (PWN) for 1 hr at 37°C, 5% CO₂. Final recovery was 42% with 89% viability. Cells were plated at 5 cells per well onto feeder cell-plated plates with 10 ng/mL human IL-2 and human IL-21. Cells were fed on day 7. 100 384-well plates were screened for binding to BSA-(Mal-(PEG)₂-VCP-eribulin). 7.7% of wells were positive for rabbit IgG production, and 68 wells were ELISA-positive for BSA-(Mal-(PEG)₂-VCP-eribulin). 50/68 hits were able to be amplified by RT-PCR and sequenced for both heavy and light chain V-regions and were subcloned into mammalian expression vectors for transient transfection in HEK-293F cells.

mRNA Gene Rescue of Rabbit Antibodies against Mal-(PEG)₂-VCP-eribulin

[00389] Total RNA was isolated from wells producing rabbit IgG anti- Mal-(PEG)₂-VCP-eribulin antibodies using RNAqueous™-96 Total RNA Isolation Kit (Ambion) according to manufacturer's instructions. cDNA was synthesized and light and heavy chain variable

regions were amplified by PCR using Platinum Taq one step RT-PCR kit (Invitrogen), according to manufacturer's instructions using in-house primers (Table 32). The light and heavy chain variable regions were amplified with nested in-house primers (Table 33) using Platinum Taq Amplification Kit using a thermocycler at 40 cycles (1 min 94°C, 1 min 54°C, 1.5 min 68°C). Amplified DNA template was visualized by gel electrophoresis, purified by QIAquick 96 PCR Purification Kit (Qiagen) and DNA sequence was determined by GeneWiz (South Plainfield, NJ) using in-house primers (Table 34). DNA Sequences were analyzed against V-gene and J-gene rabbit families (IMGT/V-QUEST) and against in-house In-Fusion primer database (Blastn). In-Fusion primers were either identified or designed containing a human Fc linker added to the 5' end for the V and J gene primer. PCR was performed with Platinum Taq Amplification Kit using a thermocycler at 40 cycles (1 min 94°C, 1 min 54°C, 1.5 min 68°C). Amplified In-Fusion DNA template was visualized on gel electrophoresis, purified by Qiagen's QIAquick 96 PCR Purification Kit. Primers were synthesized by IDT (Coralville, IA).

Table 32. Primer sequences used for one-step RT-PCR

Gene	5' Primer	3' Primer
Heavy	TYCTCCTGGTCRCTSYGCTC	TTGGTGTTGGTGGCTGGGTG
Light	GGGCCCCCACTCAGCTGCTG	GTTBTACTGKTMTYGATGCC

Table 33. Primer sequences used for PCR

Gene	5' Primer	3' Primer
Heavy	TYCTCCTGGTCRCTSYGCTC	TTGGTGTTGGTGGCTGGGTG
Light	ACTCAGCTGCTGGGGCTCCT	GTTBTACTGKTMTYGATGCC

Table 34. Primer sequences used for DNA template sequencing

Gene	3' Primer
Heavy	TTGGTGTTGGTGGCTGGGTG
Light	GTTBTACTGKTMTYGATGCC

*Methods of transient antibody productions**PCR fragments*

[00390] PCR-amplified variable domains included 15 base-pairs at the 5' and 3' ends homologous to the cloning site within the subcloning vector. PCR fragments were subcloned into an expression plasmid containing a human gamma (p1974 pC+75IZ-IIdr-InFusion-hugamma) or kappa constant region (p1975 pC+75IB-IIdr-InFusion-hukappa) using an In-Fusion HD cloning kit (Clontech) according to the manufacture's protocol. One μL of the In-Fusion reaction was transformed into Stellar Competent Cells (Clontech) according to manufacturer's protocol. Transformants were grown in 1 mL TB medium (Teknova) overnight at 37°C on a microtiter plate shaker. The next day, cultures were miniprep'd with a QIAprep 96 Turbo miniprep kit (Qiagen) using an epMotion 5075 according to the manufacture's instruction.

HEK cells

[00391] For each milliliter of 3×10^6 cells to be transfected with ExpiFectamine (ThermoFisher), 333.3 ng HC plasmid and 333.3 ng LC plasmid was incubated for 5 -10 min in 50 μL Opti-MEM (ThermoFisher). Likewise, 2.67 μL ExpiFectamine was incubated in 50 μL Opti-MEM. The ExpiFectamine solution was added to the DNA mixture and incubated for 20-30 min at room temperature. The DNA:ExpiFectamine mixture was added to the cells while swirling and incubated at 37°C, 8% CO₂, shaking at 125 rpm. The following day, 5 μL of enhancer 1 and 50 μL of enhancer 2 per mL of cells were added to the transfection with continued incubation for another 7-10 days. After 48-72 h, cells were fed at a final concentration of 10 g/L Yeastolate (BD Biosciences), 5 mM valeric acid (Sigma-Aldrich), and 1:100 CD Lipid Concentrate (ThermoFisher).

CHO cells

[00392] For each milliliter of 6×10^6 cells to be transfected with ExpiFectamine CHO (ThermoFisher), 500 ng HC plasmid and 500 ng LC plasmid was mixed in Opti-PRO (ThermoFisher) in 40 μL total volume. Likewise, 3.2 μL ExpiFectamine CHO was mixed in 36.8 μL Opti-PRO. The ExpiFectamine CHO solution was added to the DNA mixture, and incubated for 1 - 5 min at room temperature. The DNA:ExpiFectamine CHO mixture was added to the cells while swirling and incubated at 37°C, 8% CO₂, shaking at 125 rpm. The

following day, 6 μ L of enhancer and 160 μ L of feed per mL of cells were added to the transfection, and cells were transferred to 32°C, 5% CO₂. At day 5, an additional 160 μ L of feed per mL of cells was added. At day 12 to 14, the supernatants were harvested.

Methods of antibody purification

Batch purification

[00393] Prosep-vA High Capacity Protein A resin (Millipore) was equilibrated with DPBS, and 50 μ L were added to 2 mL of sample. Following incubation at room temperature for 1 hour, the medium and resin were added to a filter plate and washed twice with 1 mL DPBS. The sample was eluted from the resin by addition of 400 μ L 0.1 M glycine, pH 2.9 followed by centrifugation at 15,000 x g for 30 s. The sample was neutralized with 20 μ L of 1 M Tris, pH 8.0. The samples were concentrated to ~ 100 μ L by centrifugation at 15,000 x g for 5 minutes using 0.5 mL Amicon Ultra, 10k cutoff filters (Millipore) and were buffer exchanged into DPBS using 0.5 mL Zeba desalting columns, 7K MWCO, according to the manufacturer's protocol. MAb concentration was determined by measuring UV 280 nm absorbance and converting to mg/mL using extinction coefficient for antibody protein.

Column purification

[00394] Purification was performed using an AKTA Xpress purification platform (GE Healthcare). Up to 1 L conditioned medium was loaded onto a 1 or 5 mL MabSelect column (GE Healthcare) equilibrated in 20 mM sodium phosphate, 150 mM NaCl, pH7.0. The column was washed extensively with equilibration buffer following loading until a stable baseline was observed. Bound material was eluted using 100 mM glycine, pH 2.9. Eluted material was immediately injected on to either 2x5 mL HiTrap or 53 mL 26/10 HiPrep desalting column (GE Healthcare) equilibrated in 1x phosphate-buffered saline (PBS) and eluted in the same buffer. Peak fractions were pooled. Material was analyzed for protein content by BCA assay (ThermoFisher) and electrophoresis by reducing and non-reducing SDS-PAGE.

Antibody purification

[00395] Purification was performed using an AKTA Explorer purification platform (GE Healthcare). Up to 1 L conditioned medium was brought to 10 mM imidazole with 0.5 M

imidazole stock and loaded onto a 1 or 5 mL HisTrap column (GE Healthcare) equilibrated in 50 mM sodium phosphate, 150 mM NaCl, 10 mM imidazole, pH 7.5. The column was washed extensively with equilibration buffer following loading until a stable baseline was observed. Bound material was eluted using a linear gradient of 10 mM to 500 mM imidazole in 50 mM sodium phosphate, 150 mM NaCl, pH 7.5. Fractions were analyzed by non-reducing SDS-PAGE for the desired Fab-containing fractions. Peak fractions were pooled and dialyzed extensively against 1X DPBS at 4°C using 20 kDa MWCO dialysis cassettes. Purified material was analyzed for protein content by BCA assay (ThermoFisher) and electrophoresis by reducing and non-reducing SDS-PAGE.

ELISA

[00396] Diluted rabbit test bleeds, rabbit B-cell culture supernatants (68), or transiently-expressed In-Fusion cloned hits (50) evaluated using this assay. For test bleeds, 1:100 starting dilutions were serially diluted 2-fold). B-cell culture supernatants were used neat. For In-Fusion cloned hits, supernatants were quantitated by Octet assay using anti-human IgG biosensor tips. For ELISA, plates (384-well) were coated with BSA-[Mal-(PEG)₂-VCP-eribulin] at 0.25 µg/mL overnight and blocked with 1x assay buffer (1x PBS w/ 1% BSA, 0.05% Tween-20). Test antibody samples (20 µL/well, 100 ng/mL for In-Fusion supernatants) were added to the plate and incubated 2 hr, room temperature. Plates were washed 3X and either HRP-conjugated goat anti-rabbit Fcγ (1:20,000, Jackson Labs) for test bleeds and B-cell culture supernatants, or HRP-conjugated donkey-anti human IgG⁺M (1:10,000, Sigma) for In-Fusion supernatants, was added. Plates were incubated 1 hr at room temperature, and then washed 3X. 20 µL TMB substrate was then added and plates were incubated 7 min, then 20 µL 10% H₂SO₄ was added to stop the reaction. Plates were read at 450 nm on a Paradigm UV plate reader.

Specificity screening using Octet (BLI)

[00397] The following formats were used to screen for specificity of In-Fusion supernatants and purified antibodies:

[00398] Format #1 – Anti-human Fc biosensor tips (Pall) were wetted/blocked in 1x assay buffer (1x PBS w/ 1% BSA, 0.05% Tween-20) for > 1 hr at room temperature. Rabbit-human chimeric anti- Mal-(PEG)₂-VCP-eribulin In-Fusion cloning supernatants (used neat) or

diluted purified proteins (20 µg/mL in 1X assay buffer) were captured on biosensor tips for 200 sec at 1000 rpm shaking speed. Following antibody capture, binding to either BSA-[Mal-(PEG)₂-VCP-eribulin] (20 µg/mL in 1X assay buffer) or human serum albumin (HSA) conjugated to lysine groups with NHS-PEG₄-DBCO-N₃-PEG₄-eribulin (referred to afterward as HSA-[PEG₄-DBCO-N₃-PEG₄-eribulin], 20 µg/mL in 1X assay buffer) was observed for 150 sec at 1000 rpm shaking speed. Experiments were carried out at 25°C. Format #2 – Streptavidin-conjugated biosensor tips (Pall) were wetted/blocked in 1x assay buffer (1x PBS w/ 1% BSA, 0.05% Tween-20) for > 1 hr at room temperature. Biotinylated anti-MORAb-003 AbD14628 (BioRad, 20 µg/mL in 1X assay buffer) was captured on streptavidin biosensor tips for 150 sec at 1000 rpm shaking speed. MORAb-003, MORAb-003-[Mal-(PEG)₂-VCP-cryptophycin]₄, or MORAb-202 (20 µg/mL in 1X assay buffer) was then captured on anti-MORAb-003 for 150 sec, 1000 shaking speed. Binding of purified rabbit-human chimeric anti- Mal-(PEG)₂-VCP-eribulin clones (20 µg/mL in 1X assay buffer) was then observed for 150 sec at 1000 rpm shaking speed, followed by dissociation for 150 sec.

Spacer specificity screening of 11G6 by Octet

[00399] A reference antibody was used to generate a number of ADCs with different linkers, spacers, and cleavage sites, The ADCs were used to screen the specificity of anti-linker antibody 11G6 (list of linker payloads in FIGS. 4A, 4D. Streptavidin-conjugated biosensor tips (Pall) were wetted/blocked in 1X assay buffer (1% casein in PBS (Thermo), with 2% Tween20) for > 1 hr at room temperature. The biotinylated recombinant reference antibody extracellular domain (20 µg/mL in 1X assay buffer) was captured on streptavidin biosensor tips for 300 sec at 1000 rpm shaking speed. Reference ADCs (20 µg/mL in 1X assay buffer) were then captured on antigen-loaded tips for 300 sec, 1000 shaking speed. Binding of 11G6 (20 µg/mL in 1X assay buffer) was then observed for 300 sec at 1000 rpm shaking speed, followed binding of anti-eribulin 5E4 Fab (20 µg/mL in 1X assay buffer). Dissociation was then observed for 150 sec. Experiments were carried out at 25 °C.

Affinity determination and DAR sensitivity assessment of 5E4 by SPR

[00400] To mimic the SPR assay format (e.g., conditions) for an intact ADC immunoassay, an assay was set up to measure 5E4 binding to MORAb-003 and various DAR forms of MORAb-202, whereby biotinylated 5E4 Fab is captured on a streptavidin-coated biosensor

chip, followed by a titration of MORAb-003 and MORAb-003-based ADCs (MORAb-202 DAR variants). Biotinylated anti-eribulin antibodies AbD26976 and AbD26978 generated by phage display (BioRad) were included as positive-control comparators. 5E4, AbD26976, and AbD26978 were adjusted to 2 µg/ml in HBS-P+ buffer (GE Healthcare). Streptavidin (CAP reagent) was captured on a CAP chip (GE Healthcare) by injection across all four flow cells at 2 µL/min for 300 sec on a BIAcore T100 (GE Healthcare). Anti-eribulin antibodies were captured on the CAP chip by injection of each antibody onto flow cells 2, 3, and 4, respectively, for 100 sec at 10 µL/min. To record the antigen association to the captured anti-eribulin antibodies, a series of increasing concentrations of analyte was injected for 300 sec at a flow rate of 30 µL/min. Analyte concentrations evaluated were 200 nM, 40 nM, 8 nM, 1.6 nM, 0.32 nM, and 0 nM (buffer). The dissociation of bound analyte was monitored for 300 sec at the same flow rate. The sensor surface was regenerated by injecting 6M GuHCl, 250 mM NaOH for 120 sec at a flow rate of 30 µL/min. Sensograms were analyzed with Biacore T100 Evaluation Software using a 1:1 Langmuir binding model. Analytes evaluated were MORAb-003, MORAb-202 DAR0, DAR2, and DAR4 (all purified by HIC-HPLC), and MORAb-202 drug substance (average DAR of 4.0).

Assay methods for intact ADCs

[00401] Methods for intact ADC assays followed the procedures described below.

MORAb-202 total antibody and intact ADC assays

[00402] MORAb-202 total antibody and intact ADC assays were performed on a Gyros xPand nanoliter-scale microfluidics immunoassay instrument platform. BioAffy 4000 CDs (microfluidic assay discs) containing streptavidin were allowed to equilibrate to room temperature for at least one hour. Test plasma samples (human, cynomolgus monkey, or mouse) were first diluted 1:10 in 2% Tween 20 in REXXIP HN buffer (Gyros Protein Technologies, P0004996), then further diluted in 2% Tween 20 in REXXIP HN to bring into quantitative range of assay based on estimated concentration. For total antibody assay standard curve, MORAb-202 was first diluted to 500 ng/mL in REXXIP HN buffer from 50 µg/mL stock, then diluted 4.5-fold 6 times (range of 500 ng/mL 0.06 ng/mL, total of 7 standards). To generate an intact ADC assay standard curve, MORAb-202 was first diluted to 2000 ng/mL in REXXIP HN buffer from 50 µg/mL stock, then diluted 3-fold 6 times (range of

500 ng/mL to 2.74 ng/mL, total of 7 standards). For the total antibody assay, capture reagent was biotinylated anti-MORAb-003 Fab2 fragment 14628 (BioRad) 25 µg/mL in 2% Tween-20 in REXXIP HN buffer, detection reagent was Alexa-Fluor 647 – labeled anti-human IgG Fc (CH2 domain) (BioRad) 20 µg/mL in REXXIP F buffer (Gyros Protein Technologies, P0004825). For the intact ADC assay, capture reagent was biotinylated anti-eribulin 5E4 Fab fragment 25 µg/mL in 2% Tween-20 in REXXIP HN buffer, detection reagent was Alexa-Fluor 647 – labeled anti-MORAb-003 2G9 20 µg/mL in REXXIP F buffer. All samples and standards were centrifuged for 5 min at 5,000 x g. The following protocol was then run on the Gyros xPand for both total antibody and intact ADC assays, with a 2 nL/sec flow rate (200 nL volume for washes and reagent treatments):

- Needle was washed with Gyros wash buffer pH 11 (Gyros Protein Technologies, P0020096), then PBST
- Columns were washed 2x with PBST
- Capture reagent was passed over columns
- Columns were washed 2x with PBST
- Test samples and standards were passed over columns
- Columns were washed 2x with PBST
- Background was set prior to addition of detection reagent
- Detection reagent was passed over columns
- Columns were washed 4x with PBST
- Total captured signal was detected with 1% PMT setting
- Needle was washed with Gyros wash buffer pH 11, then PBST

[00403] Data was analyzed using the Gyros Evaluator software using a 5-parameter curve fit with response weighting, or using Watson LIMS a 5-parameter curve fit with 1/y² weighting for the standard curve.

MORAb-109 total antibody and intact ADC assays

[00404] MORAb-109 total antibody and intact ADC assays were performed on a Gyros xPand nanoliter-scale microfluidics immunoassay instrument platform. BioAffy 200 CDs containing streptavidin were allowed to equilibrate to room temperature for at least 30 min. Test plasma samples (human, cynomolgus monkey, rat, or mouse) were first diluted 1:20 in

2% Tween 20 in REXXIP HN buffer, then further diluted in 2% Tween 20 in REXXIP HN to bring into quantitative range of assay based on estimated concentration. Test tumor or tissue lysate samples (mouse) were first diluted 1:500 in 2% Tween 20 in REXXIP HN buffer, then further diluted in 2% Tween 20 in REXXIP HN to bring into quantitative range of assay based on estimated concentrations. For both the total antibody assay and intact ADC standard curves, MORAb-109 was first diluted to 800 ng/mL in REXXIP HN buffer from 50 µg/mL stock, then diluted 2.2-fold 6 times (range of 800 ng/mL 7.06 ng/mL, total of 7 standards). For the total antibody assay, capture reagent was biotinylated anti-345A12 Fab fragment @ 25 µg/mL in 2% Tween-20 in REXXIP HN buffer, detection reagent was Alexa-Fluor 647 – labeled mouse anti-human IgG Fc (Southern Biotech 9040-01) @ 20 µg/mL in REXXIP F buffer. For the intact ADC assay, capture reagent was biotinylated anti-eribulin 5E4 Fab fragment 25 µg/mL in 2% Tween-20 in REXXIP HN buffer, detection reagent was Alexa-Fluor 647 – labeled mouse anti-anti human IgG Fc @ 20 µg/mL in REXXIP F buffer. All samples and standards were centrifuged for 5 min at 5,000 x g. The following protocol was then run on the Gyros xPAND for both total antibody and intact ADC assays, with a 2 nL/sec flow rate (200 nL volume for washes and reagent treatments):

- Needle was washed with Gyros wash buffer pH 11 (Gyros Protein Technologies, P0020096), then PBST
- Columns were washed 2x with PBST
- Capture reagent was passed over columns
- Columns were washed 2x with PBST
- Test samples and standards were passed over columns
- Columns were washed 2x with PBST
- Background was set prior to addition of detection reagent
- Detection reagent was passed over columns
- Columns were washed 4x with PBST
- Total captured signal was detected with 5% PMT setting
- Needle was washed with Gyros wash buffer pH 11, then PBST

[00405] Data was analyzed using the Gyros Evaluator software using a 5-parameter curve fit with response weighting, or using Watson LIMS using a 5% PMT setting and a 5-parameter curve fit with 1/y² weighting for the standard curve.

*Assay development and format for linker-payload**Immunodepletion of MORAb-202 from plasma samples*

[00406] In order to quantitate total non-ADC Mal-(PEG)₂-VCP-eribulin, VCP-eribulin – conjugated ADC was first removed from plasma (human, cynomolgus monkey, rat, or mouse) or other matrix samples by immunodepletion. Plasma samples were diluted at least 1:500 in 2% Tween-20 in REXXIP HN. To prepare anti-MORAb-003 2G9 – coated immunocapture magnetic beads for immunodepletion, 100 µL PureProteome Streptavidin Magnetic Beads (Millipore, LSKMAGT) was washed 3 times with 500 µL PBST on a KingFisher Apex (Thermo-Fisher), then incubated in biotinylated anti-MORAb-003 (2G9) @ 100µL/well @ 400µg/mL for at least 1 hour, then collected and washed twice in 500 µL PBST. Coated beads were then added to 75 µL sample and mixed for 1 hr at room temperature. Beads were collected, incubated in 200 µL 1% acetic acid for 5 min to strip bound MORAb-202, washed twice with 500 µL PBST, then added back to the 75 µL sample. This process was repeated twice more for a total of three regeneration cycles. The immunodepleted diluted plasma sample was then used for analysis of total Mal-(PEG)₂-VCP-eribulin and albumin-conjugated Mal-(PEG)₂-VCP-eribulin. Residual MORAb-202 remaining after 3 cycles of immunodepletion was quantitated using MORAb-202 Total Antibody assay. Efficiency of immunodepletion was typically > 99.95%.

Immunodepletion of MORAb-109 from plasma samples

[00407] Plasma samples were diluted 1:5000 in 2% Tween-20 in REXXIP HN. Mouse anti-human IgG Fc-coated immunocapture magnetic beads were prepared for immunodepletion. 100 µL PureProteome Streptavidin Magnetic Beads (Millipore, LSKMAGT) were washed 3 times with 500 µL PBST on a KingFisher Apex (Thermo-Fisher), then incubated in biotinylated mouse anti Human IgG Fc (Southern Biotech, 9040-01) @ 100µL/well @ 400µg/mL for at least 1 hour, then collected and washed twice in 500 µL PBST. Coated beads were then added to 75 µL sample and mixed for 1 hr at room temperature. Beads were collected, incubated in 500 µL 1% acetic acid for 5 min to strip bound MORAb-109, washed twice with 500 µL PBST, then added back to the 75 µL sample. This process was repeated twice more for a total of three regeneration cycles. The immunodepleted diluted plasma sample was then used for analysis of total Mal-(PEG)₂-VCP-eribulin and albumin-conjugated

Mal-(PEG)₂-VCP-eribulin. Residual MORAb-109 remaining after 3 cycles of immunodepletion was quantitated using the MORAb-109 Total Antibody assay. Efficiency of immunodepletion was typically > 99%.

Generic VCP-eribulin assay

[00408] Total Mal-(PEG)₂-VCP-eribulin assays were performed on a Gyros xPanda nanoliter-scale microfluidics immunoassay instrument platform. BioAffy 4000nL CDs containing streptavidin were allowed to equilibrate to room temperature for at least 30 minutes. Test diluted (1:5000) immunodepleted plasma samples (human, cynomolgus monkey, or mouse) were further diluted in 2% Tween 20 in REXXIP HN to bring into quantitative range of assay based on estimated concentrations. Stock Mal-(PEG)₂-VCP-eribulin was diluted to 100 µg/mL in 0.3 mM N-acetylcysteine in water and incubated for 30 min to inactivate maleimide group, then diluted to a working stock of 1 µg/mL in 2% Tween 20 in REXXIP HN. 1 µg/mL stock was diluted to 10 ng/mL in 2% Tween 20 in REXXIP HN then serially-diluted 3.55-fold for a total of 7 dilutions (10,000 pg/mL – 5 pg/mL range). Capture reagent was biotinylated anti-eribulin 5E4 Fab fragment 25 µg/mL in 2% Tween-20 in REXXIP HN buffer, detection reagent was Alexa-Fluor 647 – labeled anti-VCP 11G6 @ 10 µg/mL in REXXIP F buffer. All samples and standards were centrifuged for 5 min at 5,000 x g. The following protocol was then run on the Gyros xPanda with a 2 nL/sec flow rate (200 nL volume for washes and reagent treatments):

- Needle was washed with Gyros wash buffer pH 11 (Gyros Protein Technologies, P0020096), then PBST
- Columns were washed 2x with PBST
- Capture reagent was passed over columns
- Columns were washed 2x with PBST
- Test samples and standards were passed over columns
- Columns were washed 2x with PBST
- Background was set prior to addition of detection reagent
- Detection reagent was passed over columns
- Columns were washed 4x with PBST
- Total captured signal was detected with 1% PMT setting
- Needle was washed with Gyros wash buffer pH 11, then PBST.

[00409] Data was analyzed using the Gyros Evaluator software using a 5-parameter curve fit with response weighting, or using Watson LIMS using a 5-parameter curve fit with 1/y² weighting for the standard curve.

Eribulin-conjugated albumin

[00410] Immunodepleted plasma samples were used for quantitation of eribulin-conjugated albumin from either human, cynomolgus monkey, rat, or mouse plasma. Assays were performed on a Gyros xPand nanoliter-scale microfluidics immunoassay instrument platform. For generation of standard curve samples, Mal-(PEG)₂-VCP-eribulin was spiked into species-specific plasma at 100 µg/mL, then incubated at 37 °C for at least 48 hours. Albumin-eribulin conjugate was then immunopurified from matrix using 5E4-affinity chromatography, characterized for identity by mass spectrometry, and concentration in serum was estimated by densitometry of Coomassie-stained SDS-PAGE analysis of purified samples. Standards were then generated by dilution of spiked plasma to 10 ng/mL linker-payload equivalents in 2% Tween 20 in Rxxip HN then serially-diluted 3.55-fold for a total of 7 dilutions (10,000 pg/mL – 5 pg/mL range). Capture reagent was biotinylated anti-eribulin 5E4 Fab fragment 25 µg/mL in 2% Tween-20 in Rxxip HN buffer. Detection reagents were species-specific Alexa-Fluor 647 – labeled anti-albumin antibodies) @ 10 µg/mL in 2% Tween-20 in Rxxip F buffer. Unlabeled antibodies used for - Alexa-Fluor 647 labeling were:

- Goat anti-mouse albumin – (Invitrogen, cat# PA1-30899)
- Sheep anti-rat albumin (BioRad, cat# 0200-2424)
- Goat anti-human albumin (Southern Biotech, cat# 2080-01) – used for both monkey and human albumin assays.

[00411] All samples and standards were centrifuged for 5 min at 5,000 x g. The following protocol was then run on the Gyros xPand with a 2 nL/sec flow rate (200 nL volume for washes and reagent treatments):

- Needle was washed with Gyros wash buffer pH 11 (Gyros Protein Technologies, P0020096), then PBST
- Columns were washed 2x with PBST
- Capture reagent was passed over columns
- Columns were washed 2x with PBST

- Test samples and standards were passed over columns
- Columns were washed 2x with PBST
- Background was set prior to addition of detection reagent
- Detection reagent was passed over columns
- Columns were washed 4x with PBST
- Total captured signal was detected with 1% PMT setting
- Needle was washed with Gyros wash buffer pH 11, then PBST

[00412] Data was analyzed using the Gyros Evaluator software using a 5-parameter curve fit with response weighting or using Watson LIMS using a 5-parameter curve fit with $1/y^2$ weighting for the standard curve.

Assay format for analysis of eribulin-conjugated species by IHC

[00413] The anti-eribulin antibody 5E4 was biotinylated for use in immunofluorescent staining assays to detect eribulin conjugates in formalin-fixed paraffin-embedded (FFPE) tumor samples. Briefly, after being warmed to 60 °C, the slides were deparaffinized in xylene and rehydrated by progressive immersion in ethanol (100%-95%-80%). Antigen retrieval was performed by steaming slides at 95 °C in Diva Decloaker solution for 15 minutes. Following general protein blocking (10% normal goat serum), slides were incubated in Streptavidin Blocking Solution followed by incubation in Avidin Blocking Solution (Endogenous Biotin Blocking Kit, Invitrogen). Slides were incubated with 5E4-biotin for 30 minutes followed by AlexaFluor555 conjugated Streptavidin (Invitrogen). The specimen is then counterstained using a DAPI containing mount (Prolong Gold, Invitrogen) and cover slipped. All stained slides were scanned by Panoramic Midi Fluorescence slide scanner (3DHISTECH, HUNGARY).

Analytical workflow diagrams

[00414] Analytical workflow diagrams are shown for assays described above in FIG. 23.

CLAIMS

1. A method for detecting a metabolite of an antibody-drug conjugate, wherein the metabolite is a linker-payload and the payload moiety is eribulin, the method comprising:
 - a) obtaining a biological sample from a subject who has been administered the antibody-drug conjugate;
 - b) contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the antibody-drug conjugate and/or an unconjugated antibody or antigen-binding fragment;
 - c) contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to the payload moiety of the linker-payload;
 - d) contacting the biological sample with a third antibody or antigen-binding fragment, wherein the third antibody or antigen-binding fragment is capable of specifically binding to the linker of the linker-payload; and
 - e) detecting a signal from the third antibody or antigen-binding fragment, thereby detecting the metabolite in the biological sample.
2. A method for detecting a metabolite of an antibody-drug conjugate, wherein the metabolite is a linker-payload and the payload moiety is eribulin, the method comprising:
 - a) obtaining a biological sample from a subject who has been administered the antibody-drug conjugate;
 - b) contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the antibody-drug conjugate and/or an unconjugated antibody or antigen-binding fragment;
 - c) contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to the payload moiety of the linker-payload;
 - d) contacting the biological sample with a third antibody or antigen-binding fragment, wherein the third antibody or antigen-binding fragment is capable of specifically binding to albumin; and
 - e) detecting a signal from the third antibody or antigen-binding fragment, thereby detecting the metabolite in the biological sample.

3. The method of claim 1 or claim 2, wherein the contacting of the biological sample with the first antibody immunodepletes intact antibody-drug conjugate from the biological sample.
4. The method of any one of claims 1 to 3, wherein the first, second, and/or third antibody or antigen-binding fragment is conjugated to a detectable label, a biotin, or a bead, optionally wherein
- (a) the first antibody or antigen-binding fragment is conjugated to a biotin or a bead, preferably a magnetic bead;
 - (b) the second antibody or antigen-binding fragment is conjugated to a biotin; and/or
 - (c) the third antibody or antigen-binding fragment is conjugated to a detectable label, optionally wherein the detectable label is a fluorescent tag;
- optionally wherein the first and/or second antibody or antigen-binding fragment is immobilized on a solid support.
5. The method of claim 4, wherein detecting the metabolite comprises detecting a signal from the detectable label on the third antibody or antigen-binding fragment.
6. The method of any one of claims 1 to 5, wherein the antibody-drug conjugate comprises an anti-folate receptor alpha (FRA) antibody or antigen-binding fragment, and/or the unconjugated antibody or antigen-binding fragment is an anti-FRA antibody or a fragment thereof,
- optionally wherein the antibody-drug conjugate comprises farletuzumab or an antigen-binding fragment thereof, and/or the unconjugated antibody or antigen-binding fragment is farletuzumab or a fragment thereof.
7. The method of any one of claims 1 to 6, wherein the first antibody or antigen-binding fragment specifically binds an anti-FRA antibody or antigen-binding fragment thereof, optionally wherein the first antibody or antigen-binding fragment specifically binds farletuzumab or a fragment thereof.

8. The method of claim 7, wherein the first antibody or antigen-binding fragment comprises:

(a) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 13, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 14; or

(b) three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 1 (HCDR1), SEQ ID NO: 2 (HCDR2), and SEQ ID NO: 3 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 4 (LCDR1), SEQ ID NO: 5 (LCDR2), and SEQ ID NO: 6 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 7 (HCDR1), SEQ ID NO: 8 (HCDR2), and SEQ ID NO: 9 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 10 (LCDR1), SEQ ID NO: 11 (LCDR2), and SEQ ID NO: 12 (LCDR3), as defined by the IMGT numbering system.

9. The method of claim 7 or claim 8, wherein the first antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 13, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 14,

optionally wherein the first antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 15, and a light chain comprising an amino acid sequence of SEQ ID NO: 16.

10. The method of any one of claims 7 to 9, wherein the first antibody is 2G9.

11. The method of any one of claims 1 to 5, wherein the antibody-drug conjugate comprises an anti-mesothelin (MSLN) antibody or antigen-binding fragment, and/or the unconjugated antibody or antigen-binding fragment is an anti-MSLN antibody or a fragment thereof,

optionally wherein the antibody-drug conjugate comprises 345A12-HC15-LC4 or an antigen-binding fragment thereof, and/or the unconjugated antibody or antigen-binding fragment is 345A12-HC15-LC4 or a fragment thereof.

12. The method of any one of claims 1 to 5 or 11, wherein the first antibody or antigen-binding fragment specifically binds an anti-MSLN antibody or antigen-binding fragment, optionally wherein the first antibody or antigen-binding fragment specifically binds 345A12-HC15-LC4 or a fragment thereof.

13. The method of claim 12, wherein the first antibody or antigen-binding fragment comprises

(a) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286; or

(b) three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 273 (HCDR1), SEQ ID NO: 274 (HCDR2), and SEQ ID NO: 275 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 276 (LCDR1), SEQ ID NO: 277 (LCDR2), and SEQ ID NO: 278 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 279 (HCDR1), SEQ ID NO: 280 (HCDR2), and SEQ ID NO: 281 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 282 (LCDR1), SEQ ID NO: 283 (LCDR2), and SEQ ID NO: 284 (LCDR3), as defined by the IMGT numbering system.

14. The method of claim 12 or claim 13, wherein the first antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286,

optionally wherein the first antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 287, and a light chain comprising an amino acid sequence of SEQ ID NO: 288.

15. The method of any one of claims 1 to 5, wherein the first antibody or antigen-binding fragment is an anti-human IgG Fc antibody or antigen-binding fragment thereof.

16. The method of any one of claims 1 to 15, wherein the second antibody or antigen-binding fragment comprises

(a) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 29, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 30; or

(b) three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 17 (HCDR1), SEQ ID NO: 18 (HCDR2), and SEQ ID NO: 19 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 20 (LCDR1), SEQ ID NO: 21 (LCDR2), and SEQ ID NO: 22 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 23 (HCDR1), SEQ ID NO: 24 (HCDR2), and SEQ ID NO: 25 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 26 (LCDR1), SEQ ID NO: 27 (LCDR2), and SEQ ID NO: 28 (LCDR3), as defined by the IMGT numbering system.

17. The method of claim 15 or claim 16, wherein the second antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 29, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 30,

optionally wherein the second antibody or antigen-binding fragment is an antigen-binding fragment, preferably a Fab fragment,

optionally wherein the second antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 31 or SEQ ID NO: 294, and a light chain comprising an amino acid sequence of SEQ ID NO: 32.

18. The method of any one of claims 15 to 17, wherein the second antibody or antigen-binding fragment is 5E4.

19. The method of any one of claims 1 to 18, wherein the linker-payload comprises Val-Cit-pAb-eribulin ("VCP-eribulin"), optionally wherein the third antibody or antigen-binding fragment specifically binds Val-Cit-pAB ("VCP").

20. The method of claim 19, wherein the linker-payload comprises Mal-(PEG)₂-VCP-eribulin, optionally wherein the Mal moiety is conjugated to albumin.

21. The method of claim 19 or claim 20, wherein the third antibody or antigen-binding fragment comprises

(a) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 45, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 46; or

(b) three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 33 (HCDR1), SEQ ID NO: 34 (HCDR2), and SEQ ID NO: 35 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 36 (LCDR1), SEQ ID NO: 37 (LCDR2), and SEQ ID NO: 38 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 39 (HCDR1), SEQ ID NO: 40 (HCDR2), and SEQ ID NO: 41 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 42 (LCDR1), SEQ ID NO: 43 (LCDR2), and SEQ ID NO: 44 (LCDR3), as defined by the IMGT numbering system.

22. The method of any one of claims 19 to 21, wherein the third antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 45, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 46,

optionally wherein the third antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 47, and a light chain comprising an amino acid sequence of SEQ ID NO: 48.

23. The method of any one of claims 19 to 22, wherein the third antibody or antigen-binding fragment is 11G6.

24. A method for detecting a metabolite of an antibody-drug conjugate, wherein the metabolite is a linker-payload comprising Val-Cit-pAB-eribulin (“VCP-eribulin”) and the payload moiety is eribulin, wherein the antibody-drug conjugate is MORAb-202, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-202;
 - b) contacting the biological sample with 2G9;
 - c) contacting the biological sample with 5E4;
 - d) contacting the biological sample with 11G6; and
 - e) detecting a signal from 11G6,
- thereby detecting the metabolite in the biological sample.

25. A method for detecting a metabolite of an antibody-drug conjugate, wherein the metabolite is a linker-payload comprising Val-Cit-pAB-eribulin (“VCP-eribulin”) and the payload moiety is eribulin, wherein the antibody-drug conjugate is MORAb-202, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-202;
- b) contacting the biological sample with 2G9;
- c) contacting the biological sample with 5E4;
- d) contacting the biological sample with an anti-albumin antibody; and

- e) detecting a signal from the anti-albumin antibody,
thereby detecting the metabolite in the biological sample.

26. A method for detecting a metabolite of an antibody-drug conjugate, wherein the metabolite is a linker-payload comprising Val-Cit-pAB-eribulin (“VCP-eribulin”) and the payload moiety is eribulin, wherein the antibody-drug conjugate is MORAb-109, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-109;
- b) contacting the biological sample with a first antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment comprises an anti-human IgG Fc or an anti-idiotypic antibody or antigen binding fragment, wherein the anti-idiotypic antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286;
- c) contacting the biological sample with 5E4;
- d) contacting the biological sample with 11G6; and
- e) detecting a signal from 11G6,
thereby detecting the metabolite in the biological sample.

27. A method for detecting a metabolite of an antibody-drug conjugate, wherein the metabolite is a linker-payload comprising Val-Cit-pAB-eribulin (“VCP-eribulin”) and the payload moiety is eribulin, wherein the antibody-drug conjugate is MORAb-109, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-109;
- b) contacting the biological sample with a first antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment comprises an anti-human IgG Fc or an anti-idiotypic antibody or antigen binding fragment, wherein the anti-idiotypic antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286;

- c) contacting the biological sample with 5E4;
- d) contacting the biological sample with an anti-albumin antibody; and
- e) detecting a signal from the anti-albumin antibody,
thereby detecting the metabolite in the biological sample.

28. A method for detecting total antibody-drug conjugate (ADC) and/or unconjugated antibody or antigen-binding fragment, wherein the ADC is MORAb-202 and the unconjugated antibody or antigen-binding fragment is farletuzumab or an antigen-binding fragment thereof, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-202;
- b) contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC and/or an unconjugated antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment is an anti-idiotypic antibody, wherein the anti-idiotypic antibody specifically binds farletuzumab or a fragment thereof;
- c) contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to a second epitope of the antibody portion of the ADC and/or the unconjugated antibody or antigen-binding fragment, wherein the second antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment; and
- d) detecting a signal from the second antibody or antigen-binding fragment, thereby detecting the total ADC and/or unconjugated antibody or antigen-binding fragment in the biological sample.

29. A method for detecting total antibody-drug conjugate (ADC) and/or unconjugated antibody or antigen-binding fragment, wherein the ADC is MORAb-202 and the unconjugated antibody or antigen-binding fragment is farletuzumab or an antigen-binding fragment thereof, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-202;

- b) contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC and/or the unconjugated antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment;
- c) contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to a second epitope of the antibody portion of the ADC and/or the unconjugated antibody or antigen-binding fragment, wherein the second antibody or antigen-binding fragment is an anti-idiotypic antibody, wherein the anti-idiotypic antibody specifically binds farletuzumab or a fragment thereof; and
- d) detecting a signal from the second antibody or antigen-binding fragment, thereby detecting the total ADC and/or unconjugated antibody or antigen-binding fragment in the biological sample.

30. The method of claim 28 or claim 29, wherein the anti-idiotypic antibody or antigen-binding fragment comprises

(a) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 13, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 14; or

(b) three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 1 (HCDR1), SEQ ID NO: 2 (HCDR2), and SEQ ID NO: 3 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 4 (LCDR1), SEQ ID NO: 5 (LCDR2), and SEQ ID NO: 6 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 7 (HCDR1), SEQ ID NO: 8 (HCDR2), and SEQ ID NO: 9 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 10 (LCDR1), SEQ ID NO: 11 (LCDR2), and SEQ ID NO: 12 (LCDR3), as defined by the IMGT numbering system.

31. The method of any one of claims 28 to 30, wherein the anti-idiotypic antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 13, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 14,
- optionally wherein the anti-idiotypic antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 15, and a light chain comprising an amino acid sequence of SEQ ID NO: 16.
32. The method of any one of claims 28 to 31, wherein the anti-idiotypic antibody is 2G9.
33. A method for detecting total antibody-drug conjugate (ADC) and/or unconjugated antibody or antigen-binding fragment, wherein the ADC is MORAb-109 and the unconjugated antibody or antigen-binding fragment is 345A12-HC15-LC4 or an antigen-binding fragment thereof, the method comprising:
- a) obtaining a biological sample from a subject who has been administered MORAb-109;
 - b) contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC and/or the unconjugated antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment is an anti-idiotypic antibody, wherein the anti-idiotypic antibody specifically binds 345A12-HC15-LC4 or a fragment thereof;
 - c) contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to a second epitope of the antibody portion of the ADC and/or the unconjugated antibody or antigen-binding fragment, wherein the second antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment; and
 - d) detecting a signal from the second antibody or antigen-binding fragment, thereby detecting the total ADC and/or unconjugated antibody or antigen-binding fragment in the biological sample.
34. A method for detecting total antibody-drug conjugate (ADC) and/or unconjugated antibody or antigen-binding fragment, wherein the ADC is MORAb-109 and the

unconjugated antibody or antigen-binding fragment is 345A12-HC15-LC4 or an antigen-binding fragment thereof, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-109;
- b) contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC and/or the unconjugated antibody or antigen-binding fragment, wherein the first antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment;
- c) contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to a second epitope of the antibody portion of the ADC and/or the unconjugated antibody or antigen-binding fragment, wherein the second antibody or antigen-binding fragment is an anti-idiotypic antibody, wherein the anti-idiotypic antibody specifically binds 345A12-HC15-LC4 or a fragment thereof; and
- d) detecting a signal from the second antibody or antigen-binding fragment, thereby detecting the total ADC and/or antibody or antigen-binding fragment in the biological sample.

35. The method of claim 33 or claim 34, wherein the anti-idiotypic antibody or antigen-binding fragment comprises

(a) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286; or

(b) three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 273 (HCDR1), SEQ ID NO: 274 (HCDR2), and SEQ ID NO: 275 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 276 (LCDR1), SEQ ID NO: 277 (LCDR2), and SEQ ID NO: 278 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 279 (HCDR1), SEQ ID NO: 280 (HCDR2), and SEQ ID NO: 281 (HCDR3); and three light chain

complementarity determining regions comprising amino acid sequences of SEQ ID NO: 282 (LCDR1), SEQ ID NO: 283 (LCDR2), and SEQ ID NO: 284 (LCDR3), as defined by the IMGT numbering system.

36. The method of any one of claims 33 to 35, wherein the anti-idiotypic antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286,

optionally wherein the anti-idiotypic antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 287, and a light chain comprising an amino acid sequence of SEQ ID NO: 288.

37. The method of any one of claims 28 to 36, wherein

(a) the first antibody or antigen-binding fragment is conjugated to a biotin or a bead, preferably a biotin, optionally wherein the first antibody or antigen-binding fragment is immobilized on a solid support; and/or

(b) the second antibody or antigen-binding fragment is conjugated to a detectable label, optionally wherein the detectable label is a fluorescent tag.

38. A method for detecting intact antibody-drug conjugate (ADC), wherein the ADC is MORAb-202, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-202;
- b) contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to eribulin;
- c) contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC, wherein the second antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment or an anti-idiotypic antibody or antigen-binding fragment, wherein the anti-idiotypic antibody specifically binds farletuzumab or a fragment thereof; and
- d) detecting a signal from the second antibody or antigen-binding fragment,

thereby detecting the intact ADC in the biological sample.

39. A method for detecting intact antibody-drug conjugate (ADC), wherein the ADC is MORAb-202, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-202;
- b) contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC and/or an antigen-binding fragment thereof, wherein the first antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment or an anti-idiotypic antibody or antigen-binding fragment, wherein the anti-idiotypic antibody specifically binds farletuzumab or a fragment thereof;
- c) contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to eribulin; and
- d) detecting a signal from the second antibody or antigen-binding fragment, thereby detecting the intact ADC in the biological sample.

40. The method of claim 38 or claim 39, wherein the anti-idiotypic antibody or antigen-binding fragment comprises

(a) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 13, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 14; or

(b) three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 1 (HCDR1), SEQ ID NO: 2 (HCDR2), and SEQ ID NO: 3 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 4 (LCDR1), SEQ ID NO: 5 (LCDR2), and SEQ ID NO: 6 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 7 (HCDR1), SEQ ID NO: 8 (HCDR2), and SEQ ID NO: 9 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 10 (LCDR1), SEQ ID

NO: 11 (LCDR2), and SEQ ID NO: 12 (LCDR3), as defined by the IMGT numbering system.

41. The method of any one of claims 38 to 40, wherein the anti-idiotypic antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 13, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 14,

optionally wherein the anti-idiotypic antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 15, and a light chain comprising an amino acid sequence of SEQ ID NO: 16.

42. The method of any one of claims 38 to 41, wherein the anti-idiotypic antibody is 2G9.

43. A method for detecting intact antibody-drug conjugate (ADC), wherein the ADC is MORAb-109, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-109;
- b) contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to eribulin;
- c) contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC, wherein the second antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment or an anti-idiotypic antibody or antigen-binding fragment, wherein the anti-idiotypic antibody specifically binds 345A12-HC15-LC4 or a fragment thereof; and
- d) detecting a signal from the second antibody or antigen-binding fragment, thereby detecting the intact ADC in the biological sample.

44. A method for detecting intact antibody-drug conjugate (ADC), wherein the ADC is MORAb-109, the method comprising:

- a) obtaining a biological sample from a subject who has been administered MORAb-109;

- b) contacting the biological sample with a first antibody or antigen-binding fragment capable of specifically binding to an antibody portion of the ADC, wherein the first antibody or antigen-binding fragment comprises an anti-human IgG Fc antibody or antigen-binding fragment or an anti-idiotypic antibody or antigen-binding fragment, wherein the anti-idiotypic antibody specifically binds 345A12-HC15-LC4 or a fragment thereof;
- c) contacting the biological sample with a second antibody or antigen-binding fragment capable of specifically binding to eribulin; and
- d) detecting a signal from the second antibody or antigen-binding fragment, thereby detecting the intact ADC in the biological sample.

45. The method of claim 43 or claim 44, wherein the anti-idiotypic antibody or antigen-binding fragment comprises

(a) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286; or

(b) three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 273 (HCDR1), SEQ ID NO: 274 (HCDR2), and SEQ ID NO: 275 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 276 (LCDR1), SEQ ID NO: 277 (LCDR2), and SEQ ID NO: 278 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 279 (HCDR1), SEQ ID NO: 280 (HCDR2), and SEQ ID NO: 281 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 282 (LCDR1), SEQ ID NO: 283 (LCDR2), and SEQ ID NO: 284 (LCDR3), as defined by the IMGT numbering system.

46. The method of any one of claims 43 to 45, wherein the anti-idiotypic antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286,

optionally wherein the anti-idiotypic antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 287, and a light chain comprising an amino acid sequence of SEQ ID NO: 288.

47. The method of any one of claims 38 to 46, wherein the first and/or second antibody or antigen-binding fragment capable of specifically binding to eribulin comprises

(a) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 29, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 30; or

(b) three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 17 (HCDR1), SEQ ID NO: 18 (HCDR2), and SEQ ID NO: 19 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 20 (LCDR1), SEQ ID NO: 21 (LCDR2), and SEQ ID NO: 22 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 23 (HCDR1), SEQ ID NO: 24 (HCDR2), and SEQ ID NO: 25 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 26 (LCDR1), SEQ ID NO: 27 (LCDR2), and SEQ ID NO: 28 (LCDR3), as defined by the IMGT numbering system.

48. The method of any one of claims 38 to 47, wherein the first and/or second antibody or antigen-binding fragment capable of specifically binding to eribulin comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 29, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 30,

optionally wherein first and/or second antibody or antigen-binding fragment capable of specifically binding to eribulin is an antigen-binding fragment, preferably a Fab fragment,

optionally wherein the first and/or second antibody or antigen-binding fragment capable of specifically binding to eribulin comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 31 or SEQ ID NO: 294, and a light chain comprising an amino acid sequence of SEQ ID NO: 32.

49. The method of any one of claims 38 to 48, wherein the first and/or second antibody or antigen-binding fragment capable of specifically binding to eribulin is 5E4.

50. The method of any one of claims 38 to 49, wherein

(a) the first antibody or antigen-binding fragment is conjugated to a biotin or a bead, preferably a biotin, optionally wherein the first antibody or antigen-binding fragment is immobilized on a solid support; and/or

(b) the second antibody or antigen-binding fragment is conjugated to a detectable label, optionally wherein the detectable label is a fluorescent tag.

51. A method for detecting intact and/or total antibody-drug conjugate (ADC) and/or a metabolite of an ADC, wherein the metabolite is unconjugated antibody or antigen-binding fragment, linker-payload, and/or free payload, comprising two or more of:

a) the method of any one of claims 1 to 27;

b) the method of any one of claims 28 to 37;

c) the method of any one of claims 38, 40 to 43, or 45 to 50;

d) the method of any one of claims 39 to 42, or 44 to 50; and

e) a method comprising quantification of free payload, wherein the free payload is eribulin, wherein the eribulin is quantified by multiple reaction monitoring.

52. An antibody or antigen-binding fragment thereof capable of binding to an antibody-drug conjugate comprising farletuzumab and/or to farletuzumab or an antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 13, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 14.

53. The antibody or antigen-binding fragment of claim 52, wherein the antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 1 (HCDR1), SEQ ID NO: 2 (HCDR2), and SEQ ID NO: 3 (HCDR3); and three light chain complementarity determining regions

comprising amino acid sequences of SEQ ID NO: 4 (LCDR1), SEQ ID NO: 5 (LCDR2), and SEQ ID NO: 6 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 7 (HCDR1), SEQ ID NO: 8 (HCDR2), and SEQ ID NO: 9 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 10 (LCDR1), SEQ ID NO: 11 (LCDR2), and SEQ ID NO: 12 (LCDR3), as defined by the IMGT numbering system.

54. The antibody or antigen-binding fragment of claim 52 or claim 53, wherein the antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 13, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 14,

optionally wherein the antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 15, and a light chain comprising an amino acid sequence of SEQ ID NO: 16.

55. An antibody or antigen-binding fragment thereof capable of binding to an antibody-drug conjugate comprising 345A12-HC15-LC4 and/or to 345A12-HC15-LC4 or an antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286.

56. The antibody or antigen-binding fragment of claim 55, wherein the antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 273 (HCDR1), SEQ ID NO: 274 (HCDR2), and SEQ ID NO: 275 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 276 (LCDR1), SEQ ID NO: 277 (LCDR2), and SEQ ID NO: 278 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 279 (HCDR1), SEQ ID NO: 280 (HCDR2), and SEQ ID NO: 281

(HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 282 (LCDR1), SEQ ID NO: 283 (LCDR2), and SEQ ID NO: 284 (LCDR3), as defined by the IMGT numbering system.

57. The antibody or antigen-binding fragment of claim 55 or claim 56, wherein the antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 285, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 286,

optionally wherein the antibody or antigen-binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 287, and a light chain comprising an amino acid sequence of SEQ ID NO: 288.

58. An antibody or antigen-binding fragment thereof capable of binding to eribulin, wherein the antibody or antigen-binding fragment comprises

(i) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 29, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 30;

(ii) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 101, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 102;

(iii) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 119, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 120;

(iv) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 137, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 138;

(v) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 153, and three light chain

complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 154;

(vi) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 169, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 170;

(vii) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 183, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 184;

(viii) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 200, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 201;

(ix) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 217, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 218; or

(x) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 234, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 235.

59. The antibody or antigen-binding fragment thereof of claim 58, wherein the antibody or antigen-binding fragment comprises

(i) three heavy chain complementarity determining regions (HCDRs) comprising amino acid sequences of SEQ ID NO: 17 (HCDR1), SEQ ID NO: 18 (HCDR2), and SEQ ID NO: 19 (HCDR3); and three light chain complementarity determining regions (LCDRs) comprising amino acid sequences of SEQ ID NO: 20 (LCDR1), SEQ ID NO: 21 (LCDR2), and SEQ ID NO: 22 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 23 (HCDR1), SEQ ID NO: 24 (HCDR2), and SEQ ID NO: 25 (HCDR3); and three light

chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 26 (LCDR1), SEQ ID NO: 27 (LCDR2), and SEQ ID NO: 28 (LCDR3), as defined by the IMGT numbering system;

(ii) three HCDRs comprising amino acid sequences of SEQ ID NO: 89 (HCDR1), SEQ ID NO: 90 (HCDR2), and SEQ ID NO: 91 (HCDR3); and three LCDRs comprising SEQ ID NO: 92 (LCDR1), SEQ ID NO: 93 (LCDR2), and SEQ ID NO: 94 (LCDR3) as defined by the Kabat numbering system; or three HCDRs comprising amino acid sequences of SEQ ID NO: 95 (HCDR1), SEQ ID NO: 96 (HCDR2), and SEQ ID NO: 97 (HCDR3); and three LCDRs comprising SEQ ID NO: 98 (LCDR1), SEQ ID NO: 99 (LCDR2), and SEQ ID NO: 100 (LCDR3) as defined by the IMGT numbering system;

(iii) three HCDRs comprising amino acid sequences of SEQ ID NO: 107 (HCDR1), SEQ ID NO: 108 (HCDR2), and SEQ ID NO: 109 (HCDR3); and three LCDRs comprising SEQ ID NO: 110 (LCDR1), SEQ ID NO: 111 (LCDR2), and SEQ ID NO: 112 (LCDR3) as defined by the Kabat numbering system; or three HCDRs comprising amino acid sequences of SEQ ID NO: 113 (HCDR1), SEQ ID NO: 114 (HCDR2), and SEQ ID NO: 115 (HCDR3); and three LCDRs comprising SEQ ID NO: 116 (LCDR1), SEQ ID NO: 117 (LCDR2), and SEQ ID NO: 118 (LCDR3) as defined by the IMGT numbering system;

(iv) three HCDRs comprising amino acid sequences of SEQ ID NO: 125 (HCDR1), SEQ ID NO: 126 (HCDR2), and SEQ ID NO: 127 (HCDR3); and three LCDRs comprising SEQ ID NO: 128 (LCDR1), SEQ ID NO: 129 (LCDR2), and SEQ ID NO: 130 (LCDR3) as defined by the Kabat numbering system; or three HCDRs comprising amino acid sequences of SEQ ID NO: 131 (HCDR1), SEQ ID NO: 132 (HCDR2), and SEQ ID NO: 133 (HCDR3); and three LCDRs comprising SEQ ID NO: 134 (LCDR1), SEQ ID NO: 135 (LCDR2), and SEQ ID NO: 136 (LCDR3) as defined by the IMGT numbering system;

(v) three HCDRs comprising amino acid sequences of SEQ ID NO: 143 (HCDR1), SEQ ID NO: 144 (HCDR2), and SEQ ID NO: 145 (HCDR3); and three LCDRs comprising SEQ ID NO: 146 (LCDR1), SEQ ID NO: 129 (LCDR2), and SEQ ID NO: 147 (LCDR3) as defined by the Kabat numbering system; or three HCDRs comprising amino acid sequences of SEQ ID NO: 148 (HCDR1), SEQ ID NO: 149 (HCDR2), and SEQ ID NO: 150 (HCDR3); and three LCDRs comprising SEQ ID NO: 151 (LCDR1), SEQ ID NO: 135 (LCDR2), and SEQ ID NO: 152 (LCDR3) as defined by the IMGT numbering system;

(vi) three HCDRs comprising amino acid sequences of SEQ ID NO: 159 (HCDR1), SEQ ID NO: 160 (HCDR2), and SEQ ID NO: 161 (HCDR3); and three LCDRs comprising SEQ ID NO: 162 (LCDR1), SEQ ID NO: 21 (LCDR2), and SEQ ID NO: 163 (LCDR3) as defined by the Kabat numbering system; or three HCDRs comprising amino acid sequences of SEQ ID NO: 164 (HCDR1), SEQ ID NO: 165 (HCDR2), and SEQ ID NO: 166 (HCDR3); and three LCDRs comprising SEQ ID NO: 167 (LCDR1), SEQ ID NO: 27 (LCDR2), and SEQ ID NO: 168 (LCDR3) as defined by the IMGT numbering system;

(vii) three HCDRs comprising amino acid sequences of SEQ ID NO: 175 (HCDR1), SEQ ID NO: 176 (HCDR2), and SEQ ID NO: 109 (HCDR3); and three LCDRs comprising SEQ ID NO: 177 (LCDR1), SEQ ID NO: 111 (LCDR2), and SEQ ID NO: 178 (LCDR3) as defined by the Kabat numbering system; or three HCDRs comprising amino acid sequences of SEQ ID NO: 179 (HCDR1), SEQ ID NO: 180 (HCDR2), and SEQ ID NO: 115 (HCDR3); and three LCDRs comprising SEQ ID NO: 181 (LCDR1), SEQ ID NO: 117 (LCDR2), and SEQ ID NO: 182 (LCDR3) as defined by the IMGT numbering system;

(viii) three HCDRs comprising amino acid sequences of SEQ ID NO: 189 (HCDR1), SEQ ID NO: 190 (HCDR2), and SEQ ID NO: 191 (HCDR3); and three LCDRs comprising SEQ ID NO: 192 (LCDR1), SEQ ID NO: 193 (LCDR2), and SEQ ID NO: 194 (LCDR3) as defined by the Kabat numbering system; or three HCDRs comprising amino acid sequences of SEQ ID NO: 195 (HCDR1), SEQ ID NO: 196 (HCDR2), and SEQ ID NO: 197 (HCDR3); and three LCDRs comprising SEQ ID NO: 198 (LCDR1), SEQ ID NO: 117 (LCDR2), and SEQ ID NO: 199 (LCDR3) as defined by the IMGT numbering system;

(ix) three HCDRs comprising amino acid sequences of SEQ ID NO: 206 (HCDR1), SEQ ID NO: 207 (HCDR2), and SEQ ID NO: 208 (HCDR3); and three LCDRs comprising SEQ ID NO: 92 (LCDR1), SEQ ID NO: 209 (LCDR2), and SEQ ID NO: 210 (LCDR3) as defined by the Kabat numbering system; or three HCDRs comprising amino acid sequences of SEQ ID NO: 211 (HCDR1), SEQ ID NO: 212 (HCDR2), and SEQ ID NO: 213 (HCDR3); and three LCDRs comprising SEQ ID NO: 214 (LCDR1), SEQ ID NO: 215 (LCDR2), and SEQ ID NO: 216 (LCDR3) as defined by the IMGT numbering system; or

(x) three HCDRs comprising amino acid sequences of SEQ ID NO: 223 (HCDR1), SEQ ID NO: 224 (HCDR2), and SEQ ID NO: 225 (HCDR3); and three LCDRs comprising SEQ ID NO: 226 (LCDR1), SEQ ID NO: 227 (LCDR2), and SEQ ID NO: 228 (LCDR3) as defined by the Kabat numbering system; or three HCDRs comprising amino acid

sequences of SEQ ID NO: 229 (HCDR1), SEQ ID NO: 230 (HCDR2), and SEQ ID NO: 231 (HCDR3); and three LCDRs comprising SEQ ID NO: 232 (LCDR1), SEQ ID NO: 99 (LCDR2), and SEQ ID NO: 233 (LCDR3) as defined by the IMGT numbering system.

60. The antibody or antigen-binding fragment thereof of claim 58 or claim 59, wherein the antibody or antigen-binding fragment comprises three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 17 (HCDR1), SEQ ID NO: 18 (HCDR2), and SEQ ID NO: 19 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 20 (LCDR1), SEQ ID NO: 21 (LCDR2), and SEQ ID NO: 22 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 23 (HCDR1), SEQ ID NO: 24 (HCDR2), and SEQ ID NO: 25 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 26 (LCDR1), SEQ ID NO: 27 (LCDR2), and SEQ ID NO: 28 (LCDR3), as defined by the IMGT numbering system.

61. The antibody or antigen-binding fragment of claim 58 or claim 59, wherein the antibody or antigen-binding fragment comprises

(i) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 29, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 30;

(ii) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 101, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 102;

(iii) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 119, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 120;

(iv) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 137, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 138;

(v) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 153, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 154;

(vi) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 169, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 170;

(vii) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 183, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 184;

(viii) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 200, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 201;

(ix) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 217, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 218; or

(x) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 234, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 235.

62. The antibody or antigen-binding fragment of any one of claims 58 to 61, wherein the antibody or antigen-binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 29, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 30.

63. The antibody or antigen-binding fragment of any one of claims 58 to 62, wherein the antibody or antigen-binding fragment is an antigen-binding fragment, preferably a Fab fragment.

64. The antibody or antigen-binding fragment of any one of claims 58 to 63, wherein the antibody or antigen-binding fragment comprises

(i) a heavy chain comprising an amino acid sequence of SEQ ID NO: 31 or 294 and a light chain comprising an amino acid sequence of SEQ ID NO: 32;

- (ii) a heavy chain comprising an amino acid sequence of SEQ ID NO: 103 and a light chain comprising an amino acid sequence of SEQ ID NO: 104;
- (iii) a heavy chain comprising an amino acid sequence of SEQ ID NO: 121 and a light chain comprising an amino acid sequence of SEQ ID NO: 122;
- (iv) a heavy chain comprising an amino acid sequence of SEQ ID NO: 139 and a light chain comprising an amino acid sequence of SEQ ID NO: 140;
- (v) a heavy chain comprising an amino acid sequence of SEQ ID NO: 155 and a light chain comprising an amino acid sequence of SEQ ID NO: 156;
- (vi) a heavy chain comprising an amino acid sequence of SEQ ID NO: 171 and a light chain comprising an amino acid sequence of SEQ ID NO: 172;
- (vii) a heavy chain comprising an amino acid sequence of SEQ ID NO: 185 and a light chain comprising an amino acid sequence of SEQ ID NO: 186;
- (viii) a heavy chain comprising an amino acid sequence of SEQ ID NO: 202 and a light chain comprising an amino acid sequence of SEQ ID NO: 203;
- (ix) a heavy chain comprising an amino acid sequence of SEQ ID NO: 219 and a light chain comprising an amino acid sequence of SEQ ID NO: 220; or
- (x) a heavy chain comprising an amino acid sequence of SEQ ID NO: 236 and a light chain comprising an amino acid sequence of SEQ ID NO: 237.

65. An antibody or antigen-binding fragment thereof capable of binding to Val-Cit-pAB ("VCP"), wherein the antibody or antigen-binding fragment comprises

- (i) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 45, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 46; or
- (ii) three heavy chain complementarity determining regions from a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 248, and three light chain complementarity determining regions from a light chain variable region comprising an amino acid sequence of SEQ ID NO: 249.

66. The antibody or antigen-binding fragment thereof of claim 65, wherein the antibody or antigen-binding fragment comprises

(i) three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 33 (HCDR1), SEQ ID NO: 34 (HCDR2), and SEQ ID NO: 35 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 36 (LCDR1), SEQ ID NO: 37 (LCDR2), and SEQ ID NO: 38 (LCDR3), as defined by the Kabat numbering system; or three heavy chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 39 (HCDR1), SEQ ID NO: 40 (HCDR2), and SEQ ID NO: 41 (HCDR3); and three light chain complementarity determining regions comprising amino acid sequences of SEQ ID NO: 42 (LCDR1), SEQ ID NO: 43 (LCDR2), and SEQ ID NO: 44 (LCDR3), as defined by the IMGT numbering system; or

(ii) three HCDRs comprising amino acid sequences of SEQ ID NO: 159 (HCDR1), SEQ ID NO: 240 (HCDR2), and SEQ ID NO: 241 (HCDR3); and three LCDRs comprising SEQ ID NO: 242 (LCDR1), SEQ ID NO: 209 (LCDR2), and SEQ ID NO: 243 (LCDR3) as defined by the Kabat numbering system; or three HCDRs comprising amino acid sequences of SEQ ID NO: 164 (HCDR1), SEQ ID NO: 244 (HCDR2), and SEQ ID NO: 245 (HCDR3); and three LCDRs comprising SEQ ID NO: 246 (LCDR1), SEQ ID NO: 215 (LCDR2), and SEQ ID NO: 247 (LCDR3) as defined by the IMGT numbering system.

67. The antibody or antigen-binding fragment of claim 65 or claim 66, wherein the antibody or antigen-binding fragment comprises

(i) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 45, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 46;

(ii) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 248, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 249;

(iii) a heavy chain comprising an amino acid sequence of SEQ ID NO: 47, and a light chain comprising an amino acid sequence of SEQ ID NO: 48; or

(iv) a heavy chain comprising an amino acid sequence of SEQ ID NO: 250, and a light chain comprising an amino acid sequence of SEQ ID NO: 251.

68. The antibody or antigen-binding fragment of any one of claims 52 to 67, wherein the antibody or antigen-binding fragment is conjugated to a label, optionally wherein the label comprises a fluorescent tag, an enzyme reporter, a biotin, or a bead.