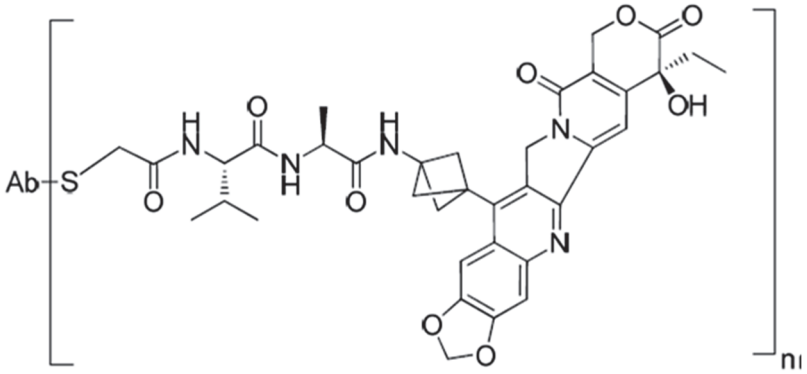
5. SUMMARY

[0008] The present disclosure provides antibody drug conjugates that specifically bind to human c-Met. The amino acid sequences of exemplary CDRs, as well as the amino acid sequence of the V_H and V_L regions of the heavy and light chains of the antibody of exemplary anti-c-Met ADCs are provided in the Detailed Description below.

[0008a] In one aspect, the present disclosure provides anti-c-Met antibody drug conjugate comprising the following structure:



wherein n is an integer from 1 to 10, and wherein Ab is an IgG1 anti-c-Met antibody comprising

a heavy chain variable region comprising a heavy chain CDR3 domain comprising the amino acid sequence shown as SEQ ID NO: 3, a heavy chain CDR2 domain comprising the amino acid sequence shown as SEQ ID NO: 2, and a heavy chain CDR1 domain comprising the amino acid sequence shown as SEQ ID NO: 1; and

a light chain variable region comprising a light chain CDR3 domain comprising the amino acid sequence shown as SEQ ID NO: 6, a light chain CDR2 domain comprising the amino acid sequence shown as SEQ ID NO: 5, and a light chain CDR1 domain comprising the amino acid sequence shown as SEQ ID NO: 4.

[0009] In another aspect, the present disclosure provides compositions including the anti-c-Met ADCs described herein. The compositions generally comprise one or more anti-c-Met ADC as described herein, and one or more excipients, carriers, or diluents.

[0010] The present disclosure provides methods of treating subjects, such as human subjects, having NSCLC comprising administering an effective amount of an anti-c-Met ADCs disclosed herein. An anti-c-Met ADC is typically administered as an intravenous infusion and/or injection.

6. BRIEF DESCRIPTION OF THE DRAWINGS

[0011] FIG. 1 shows a synthetic pathway for the topoisomerase I (TOP1) inhibitor of Formula I.

[0012] FIGS. 2A-2B show cell proliferation following administration of TOP1 inhibitor compounds for Calu-6 (lung adenocarcinoma; FIG. 2A) and A375 (malignant melanoma; FIG 2B).

[0013] FIGS. 3A-3J show in vitro activity of an ADC of the present disclosure (ADC-1) on cell lines, including (A) SNU-5 (human gastric carcinoma), (B) Hs 746T (gastric adenocarcinoma), (C) EBC1 (human lung squamous cell carcinoma), (D) NCI-H441 (human lung adenocarcinoma), (E) NCI-H1573 (lung adenocarcinoma), (F) HCC827 (lung adenocarcinoma), (G) NCI-H820 (lung papillary adenocarcinoma), (H) Calu-3 (lung adenocarcinoma), (I) MIA PaCa-2 (pancreatic ductal adenocarcinoma), and (J) HEK-293.

[0014] FIGS. 4A-4B show in vivo activity of ADC-1 in the NCI-H441 (human adenocarcinoma, FIG. 4A), and Hs 746T (gastric adenocarcinoma, FIG. 4B) xenograft tumor models.

7. DETAILED DESCRIPTION

[0015] Various aspects of the invention relate to topoisomerase I (TOP1) inhibitors and anti-c-Met antibody drug conjugates comprising such TOP1 inhibitors. In certain embodiments, the invention provides anti-c-Met ADCs, including anti-c-Met ADCs comprising TOP1 inhibitors, synthons useful for synthesizing the ADCs, methods of making the ADCs, and various methods of using the ADCs.