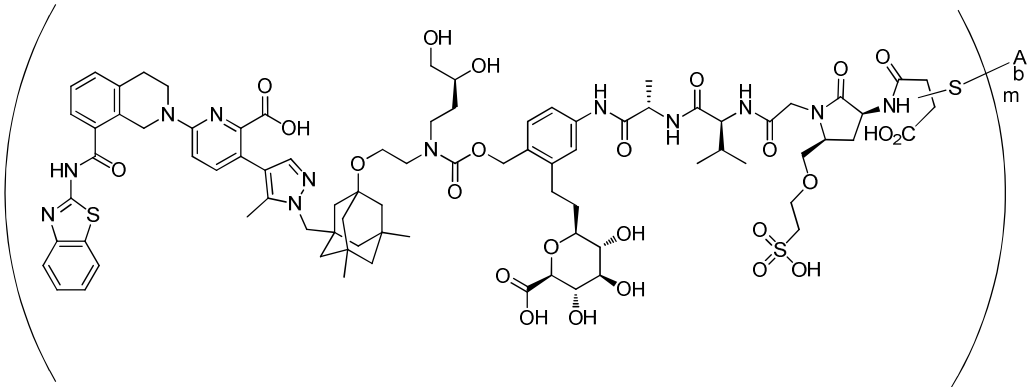
There remains a need in the art for anti-B7-H3 antibodies and anti-B7-H3 ADCs that can be used for therapeutic purposes in the treatment of cancer.

SUMMARY OF THE INVENTION

In one aspect, provided herein is an anti-hB7-H3 antibody drug conjugate comprising the following structure:



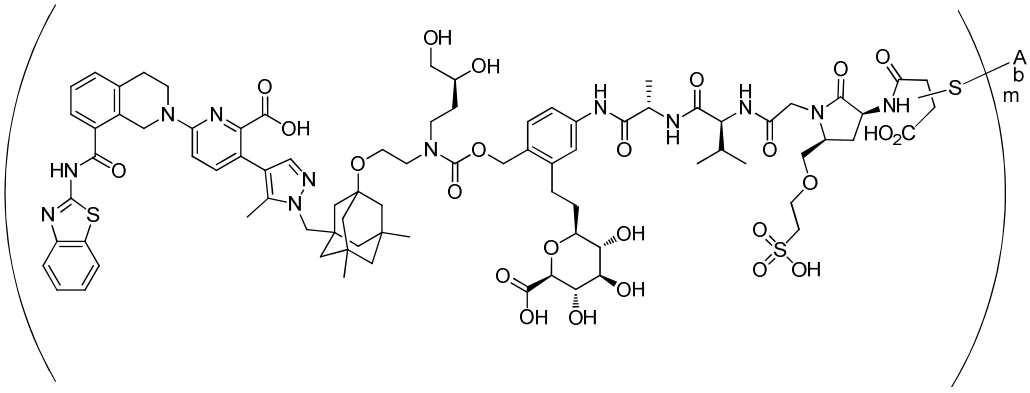
wherein Ab is an IgG1 anti-hB7-H3 antibody comprising

a heavy chain variable region comprising a heavy chain CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO: 35, a heavy chain CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO: 34, and a heavy chain CDR1 domain comprising the amino acid sequence set forth in SEQ ID NO: 33; and

a light chain variable region comprising a light chain CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO: 39, a light chain CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO: 38, and a light chain CDR1 domain comprising the amino acid sequence set forth in SEQ ID NO: 37; and

wherein m is 2.

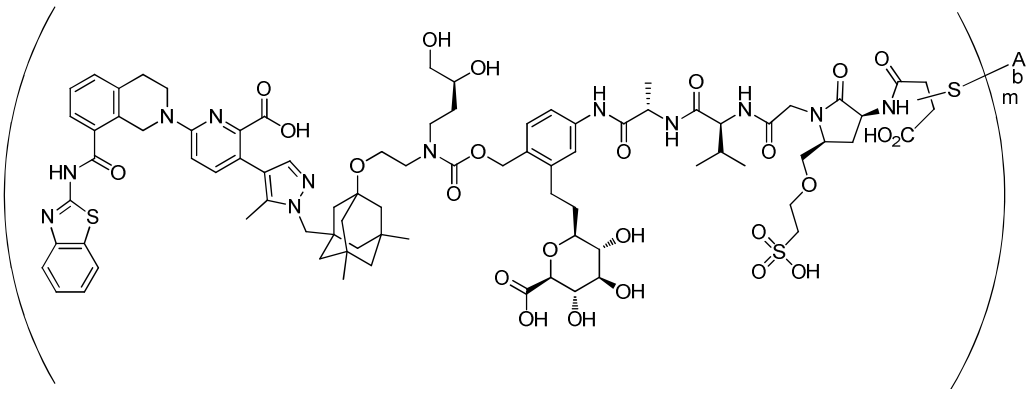
In another aspect, provided herein is an anti-hB7-H3 antibody drug conjugate comprising the following structure:



wherein Ab is an IgG1 anti-hB7-H3 antibody comprising a heavy chain variable domain comprising an amino acid sequence set forth in SEQ ID NO: 147 and a light chain variable domain comprising an amino acid sequence set forth in SEQ ID NO: 144; and

wherein m is 2.

In another aspect, provided herein is an anti-hB7-H3 antibody drug conjugate comprising the following structure:



wherein Ab is an IgG1 anti-hB7-H3 antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 168 and a light chain comprising the amino acid sequence of SEQ ID NO: 169; and

wherein m is 2.

In certain aspects, the present invention provides for antibodies and antibody drug conjugates (ADCs) that specifically bind to human B7-H3. In certain aspects, the present invention provides novel ADCs that can selectively deliver Bcl-xL inhibitors to target cancer cells, *e.g.*, B7-H3 expressing cells.

In one aspect, the present invention provides an antoi-B7-H3 antibody, or antigen binding portion thereof, that binds to human B7-H3 (hB7-H3), wherein the antibody, or antigen binding portion thereof, comprises a heavy chain variable region comprising a CDR3 having the amino acid sequence of SEQ ID NO: 12 and a light chain variable region comprising a CDR3 having the amino acid sequence of SEQ ID NO: 15.

In one embodiment, the anti-B7-H3 antibody, or antigen binding portion thereof, comprises a heavy chain variable region comprising a CDR2 having the amino acid sequence of SEQ ID NO: 140 and a light chain variable region comprising a CDR2 having the amino acid sequence of SEQ ID NO: 7.

In one embodiment, the anti-B7-H3 antibody, or antigen binding portion thereof, comprises a heavy chain variable region comprising a CDR1 having the amino acid sequence of SEQ ID NO: 10 and a light chain variable region comprising a CDR1 having the amino acid sequence of either SEQ ID NO: 136 or 138.

In one aspect, the present invention provides an anti- B7-H3 antibody, or antigen binding portion thereof, that binds to human B7-H3 (hB7-H3), wherein the antibody, or antigen binding portion thereof, comprises a heavy chain variable region comprising a CDR3 having the amino acid sequence of SEQ ID NO: 35 and a light chain variable region comprising a CDR3 having the amino acid sequence of SEQ ID NO: 39.

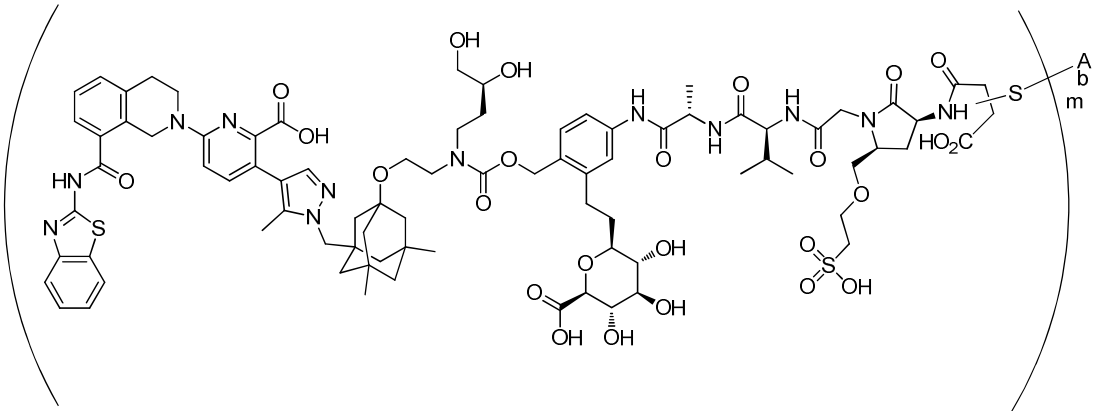
In one embodiment, the anti-B7-H3 antibody, or antigen binding portion thereof, comprises a heavy chain variable region comprising a CDR2 having the amino acid sequence of SEQ ID NO: 34, and a light chain variable region comprising a CDR2 having the amino acid sequence of SEQ ID NO: 38.

In one embodiment, the anti-B7-H3 antibody, or antigen binding portion thereof, comprises a heavy chain variable region comprising a CDR1 having the amino acid sequence of SEQ ID NO: 33 and a light chain variable region comprising a CDR1 having the amino acid sequence of either SEQ ID NO: 37.

In one embodiment, the anti-B7-H3 antibody, or antigen binding portion thereof, is an IgG isotype.

CLAIMS

1. An anti-hB7-H3 antibody drug conjugate comprising the following structure:



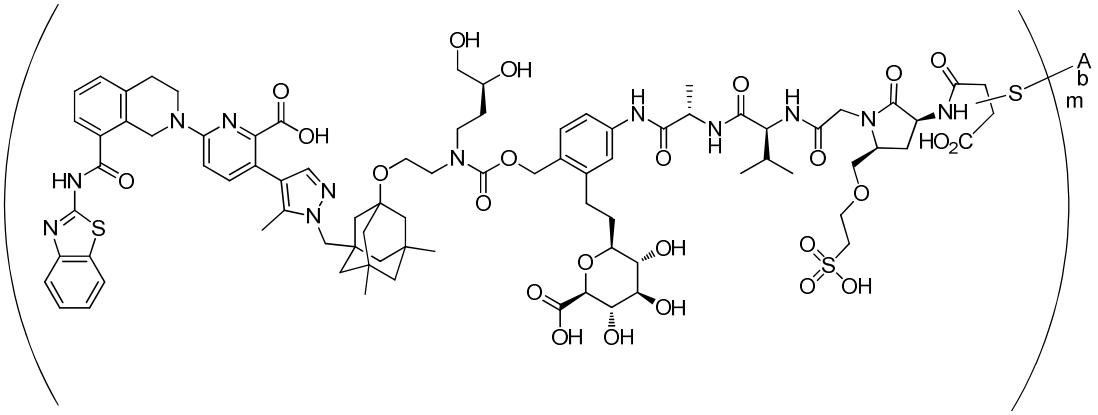
wherein Ab is an IgG1 anti-hB7-H3 antibody comprising

a heavy chain variable region comprising a heavy chain CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO: 35, a heavy chain CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO: 34, and a heavy chain CDR1 domain comprising the amino acid sequence set forth in SEQ ID NO: 33; and

a light chain variable region comprising a light chain CDR3 domain comprising the amino acid sequence set forth in SEQ ID NO: 39, a light chain CDR2 domain comprising the amino acid sequence set forth in SEQ ID NO: 38, and a light chain CDR1 domain comprising the amino acid sequence set forth in SEQ ID NO: 37; and

wherein m is 2.

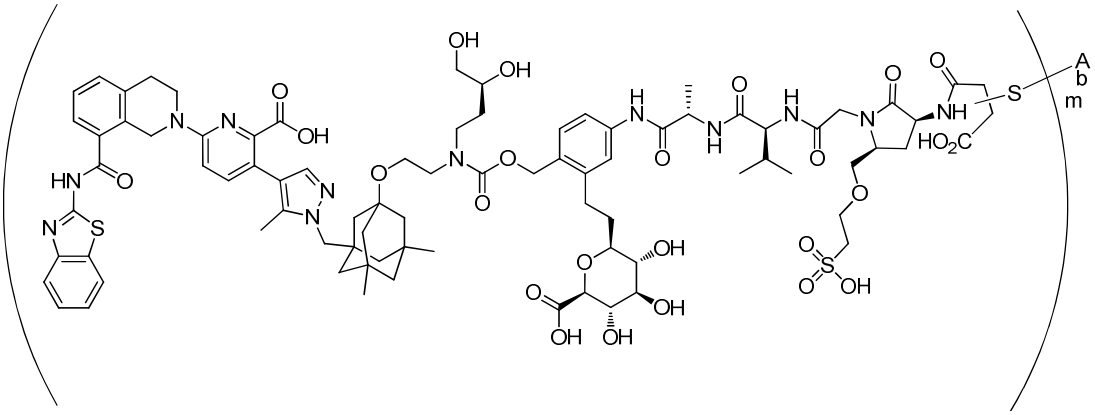
2. An anti-hB7-H3 antibody drug conjugate comprising the following structure:



wherein Ab is an IgG1 anti-hB7-H3 antibody comprising a heavy chain variable domain comprising an amino acid sequence set forth in SEQ ID NO: 147 and a light chain variable domain comprising an amino acid sequence set forth in SEQ ID NO: 144; and

wherein m is 2.

3. An anti-hB7-H3 antibody drug conjugate comprising the following structure:



wherein Ab is an IgG1 anti-hB7-H3 antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 168 and a light chain comprising the amino acid sequence of SEQ ID NO: 169; and

wherein m is 2.