Therefore, antibody–drug conjugates (ADC) have been generated (such as the humanized anti-CD79b antibody (humanized SN8) conjugated to monomethylauristatin E (MMAE) by a protease cleavable linker), which has shown to be clinical efficacious for the treatment of NHL. *See e.g.*, U.S. Patent No. 8,088,378 and Morschhauser et al., "*4457 Updated Results of a Phase II Randomized Study (ROMULUS) of Polatuzumab Vedotin or Pinatuzumab Vedotin Plus Rituximab in Patients with Relapsed/Refractory Non-Hodgkin Lymphoma*" 56th ASH Annual Meeting and Exposition: December 6-9, 2014. Despite the advances in NHL and CLL treatment using anti-CD79b ADC therapeutics, there still remains an unmet need for improved therapies for NHL and CLL patients, in particular those resistant to anti-CD79b ADC therapies.

[0007] Recently, bispecific antibody-based immunotherapies have been developed, which are capable of simultaneously binding cell surface antigens on cytotoxic cells and tumor cells with the intent that the bound cytotoxic cell will destroy the bound tumor cell. Such bispecific antibodies may have advantages, *e.g.*, efficacy and/or safety compared to the antibody-drug conjugate. Thus, there is an unmet need in the field for the development of effective bispecific antibodies for use in cancer treatment.

SUMMARY

[0008] The disclosure provides anti-CD79b antibodies and methods of using the same. In particular provided herein are anti-CD79b antibodies comprising a CD79b binding domain and a CD3 binding domain.

[0009] In one aspect, provided herein are isolated anti-CD79b antibodies, the antibody comprises a CD79b binding domain comprising the following six hypervariable regions (HVRs): (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 5; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 8; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 9; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 10; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 11; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 12.

[0010] In some embodiments, the CD79b binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 3; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 6; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 9; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 10; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 11; and (f)an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 12. In some embodiments, the anti-CD79b antibody comprises (a) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:17, 21, 23, 25, 27 or 29; (b) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:18, 22, 24, 26, 28, or 30; or (c) a VH sequence as in (a) and a VL sequence as in (b). In some embodiments, the

embodiments, cytotoxic T cell activation is measured by % of CD69+CD25+ T cells in CD8+ T cells.

[0025] In some embodiments of any of the multispecific anti-CD79b antibodies, the multispecific antibody is a bispecific antibody.

[0026] In some embodiments of any of the multispecific anti-CD79b antibodies, (a) the CD3 binding domain comprises a Fc domain, wherein the Fc domain comprises T366S, L368A, Y407V, and N297G substitution mutations according EU numbering and (b) the CD79b binding domain comprises a Fc domain, wherein the Fc domain comprises T366W and N297G substitution mutations according EU numbering. In some embodiments of any of the multispecific anti-CD79b antibodies, (a) the CD79b binding domain comprises a Fc domain, wherein the Fc domain comprises T366S, L368A, Y407V, and N297G substitution mutations according EU numbering and (b) the CD3 binding domain comprises a Fc domain, wherein the Fc domain comprises T366W and N297G substitution mutations according EU numbering.

[0027] In some embodiments of any of the multispecific anti-CD79b antibodies, the anti-CD79b antibody comprises one or more heavy chain constant domains, wherein the one or more heavy chain constant domains are selected from a first CH1 ($CH1_1$) domain, a first CH2 ($CH2_1$) domain, a first CH3 ($CH3_1$) domain, a second CH1 ($CH1_2$) domain, second CH2 ($CH2_2$) domain, and a second CH3 ($CH3_2$) domain. In some embodiments, at least one of the one or more heavy chain constant domains is paired with another heavy chain constant domain. In some embodiments, the $CH3_1$ and $CH3_2$ domains each comprise a protuberance or cavity, and wherein the protuberance or cavity in the $CH3_1$ domain is positionable in the cavity or protuberance, respectively, in the $CH3_2$ domain. In some embodiments, the $CH3_1$ and $CH3_2$ domains meet at an interface between said protuberance and cavity. In some embodiments, the $CH2_1$ and $CH2_2$ domains each comprise a protuberance or cavity, and wherein the protuberance or cavity in the $CH2_1$ domain is positionable in the cavity or protuberance, respectively, in the $CH2_2$ domain. In some embodiments, the $CH2_1$ and $CH2_2$ domains meet at an interface between said protuberance and cavity.

[0028] In one aspect, provided herein are also isolated nucleic acids encoding an anti-CD79b antibody described herein. In another aspect, further provided herein are vectors comprising an isolated nucleic acid encoding an anti-CD79b antibody described herein. In yet another aspect, provided herein are host cells comprising a vector comprising an isolated nucleic acid encoding an anti-CD79b antibody described herein. In some embodiments, the host cell is a eukaryotic host cell. In some embodiments, the host cell is a mammalian host cell (*e.g.*, CHO). In some embodiments, the host cell is a prokaryotic host cell. In some embodiments, the prokaryotic host cell is an *E. coli* host cell. In a further aspect, provided herein are methods of producing the anti-CD79b antibody described herein, wherein the method comprising culturing the host cell described herein in a culture medium.

[0029] In one aspect, provided herein are immunoconjugates comprising an anti-CD79b antibody of described herein and a cytotoxic agent.

[0030] In one aspect, provided herein are pharmaceutical compositions comprising the anti-CD79b antibody described herein.

[0031] In one aspect, provided herein are anti-CD79b antibodies as described herein for use as a medicament. In another aspect, provided herein are anti-CD79b antibody described herein for use in treating or delaying progression of a B cell proliferative disorder or an autoimmune disorder in a subject in need thereof. In yet another aspect, provided herein are anti-CD79b antibodies as described herein for use in enhancing immune function in a subject having a B cell proliferative disorder or an autoimmune disorder. In some embodiments, the B cell proliferative disorder is a cancer. In some embodiments, the B cell proliferative disorder is lymphoma, non-Hodgkins lymphoma (NHL), aggressive NHL, relapsed aggressive NHL, relapsed indolent NHL, refractory NHL, refractory indolent NHL, chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma, leukemia, hairy cell leukemia (HCL), acute lymphocytic leukemia (ALL), and/or mantle cell lymphoma. In some embodiments of any of the B cell proliferative disorders, the B cell proliferative disorder is resistant to treatment with an anti-CD79b antibody drug conjugate (*e.g.*, anti-CD79b MMAE antibody drug conjugate). In some embodiments, the autoimmune disorder is selected from the group consisting of rheumatoid arthritis, juvenile rheumatoid arthritis, systemic lupus erythematosus (SLE), Wegener's disease, inflammatory bowel disease, idiopathic thrombocytopenic purpura (ITP), thrombotic thrombocytopenic purpura (TTP), autoimmune thrombocytopenia, multiple sclerosis, psoriasis, IgA nephropathy, IgM polyneuropathies, myasthenia gravis, vasculitis, diabetes mellitus, Reynaud's syndrome, Sjorgen's syndrome, glomerulonephritis, Neuromyelitis Optica (NMO) and IgG neuropathy.

[0032] In one aspect, provided herein are uses of any of the anti-CD79b antibody described herein in the manufacture of a medicament for treating or delaying progression of a cell proliferative disorder or an autoimmune disorder. In another aspect, provided herein are uses of any of the anti-CD79b antibody described herein in the manufacture of a medicament for enhancing immune function in a subject having a cell proliferative disorder or an autoimmune disorder. In some embodiments, the B cell proliferative disorder is a cancer. In some embodiments, the B cell proliferative disorder is lymphoma, non-Hodgkins lymphoma (NHL), aggressive NHL, relapsed aggressive NHL, relapsed indolent NHL, refractory NHL, refractory indolent NHL, chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma, leukemia, hairy cell leukemia (HCL), acute lymphocytic leukemia (ALL), and/or mantle cell lymphoma. In some embodiments of any of the B cell proliferative disorders, the B cell proliferative disorder is resistant to treatment with an anti-CD79b antibody drug conjugate (*e.g.*, anti-CD79b MMAE antibody drug conjugate). In some embodiments, the autoimmune disorder is selected from the group consisting of rheumatoid arthritis, juvenile rheumatoid arthritis, systemic lupus

59. Use of the anti-CD79b antibody of any one of claims 1-46 in the manufacture of a medicament for enhancing immune function in a subject having a cell proliferative disorder or an autoimmune disorder.

60. The use of any one of claims 58-59, wherein the cell proliferative disorder is a cancer.

61. The use of any one of claims 58-60 wherein the B cell proliferative disorder is lymphoma, NHL, aggressive NHL, relapsed aggressive NHL, relapsed indolent NHL, refractory NHL, refractory indolent NHL, CLL, small lymphocytic lymphoma, leukemia, HCL, ALL, and/or mantle cell lymphoma.

62. The use of any one of claims 58-61, wherein the medicament is to be administered with a PD-1 axis binding antagonist or an additional therapeutic agent.

63. The use of any one of claims 58-62, wherein the medicament is to be administered with a glucocorticoid.

64. The use of claim 63, wherein the glucocorticoid is dexamethasone.

65. The use of any one of claims 58-64, wherein the medicament is to be administered with rituximab.