CLAIMS

1. An isolated nucleic acid molecule encoding a chimeric antigen receptor (CAR), wherein the CAR comprises a CD20 binding domain, a transmembrane domain, and an intracellular signaling domain, wherein said CD20 binding domain comprises one or more of light chain complementarity determining region 1 (LCDR1), light chain complementarity determining region 2 (LCDR2), and light chain complementarity determining region 3 (LCDR3) of any CD20 binding domain of Table 1 or Table 3, and one or more of heavy chain complementarity determining region 1 (HCDR1), heavy chain complementarity determining region 2 (HCDR2), and heavy chain complementarity determining region 3 (HCDR3) of any CD20 binding domain of Table 1 or Table 2.

2. The isolated nucleic acid molecule of claim 1, wherein:

(i) the CAR comprises a LCDR1, LCDR2, and LCDR3 according to Table 1 or Table 3;

(ii) the CAR comprises a HCDR1, HCDR2, and HCDR3 according to Table 1 or Table 2;

(iii) the CAR comprises LCDR1, LCDR2, and LCDR3 according to Table 1 or Table 3, and HCDR1, HCDR2, and HCDR3 according to Table 1 or Table 2;

(iv) the LCDR1, LCDR2, and LCDR3, respectively, is chosen from a)-p) of the following:

(a) SEQ ID NOs: 147, 148, and 149;

(b) SEQ ID NOs: 228, 229, and 230;

(c) SEQ ID NOs: 66, 67, and 68;

(d) SEQ ID NOs: 93, 94, and 95;

(e) SEQ ID NOs: 120, 121, and 122;

(f) SEQ ID NOs: 12, 13, and 14;

(g) SEQ ID NOs: 174, 175, and 176;

(h) SEQ ID NOs: 201, 202, and 203;

(i) SEQ ID NOs: 39, 40, and 41;

(j) SEQ ID NOs: 255, 256, and 257;

(k) SEQ ID NOs: 282, 283, and 284;

(l) SEQ ID NOs: 309, 310, and 311;

(m) SEQ ID NOs: 336, 337, and 338;

(n) SEQ ID NOs: 363, 364, and 365;

(o) SEQ ID NOs: 390, 391, and 392; and

(p) SEQ ID NOs: 417, 418, and 419;

(v) the HCDR1, HCDR2, and HCDR3, respectively, is chosen from a)-p) of the following:

(a) SEQ ID NOs: 136, 137, and 138;

(b) SEQ ID NOs: 217, 218, and 219;

(c) SEQ ID NOs: 55, 56, and 57;

(d) SEQ ID NOs: 82, 83, and 84;

(e) SEQ ID NOs: 109, 110, and 111;

(f) SEQ ID NOs: 1, 2, and 3;

(g) SEQ ID NOs: 163, 164, and 165;

(h) SEQ ID NOs: 190, 191, and 192;

(i)SEQ ID NOs: 28, 29, and 30;

(j) SEQ ID NOs: 244, 245, and 246;

(k) SEQ ID NOs: 271, 272, and 273;

(l) SEQ ID NOs: 298, 299, and 300;

(m) SEQ ID NOs: 325, 326, and 327;

(n) SEQ ID NOs: 352, 353, and 354;

(o) SEQ ID NOs: 379, 380, and 381; and

(p) SEQ ID NOs: 406, 407, and 408; or

(vi) the LCDR1, LCDR2, LCDR3, HCDR1, HCDR2, and HCDR3, respectively, is chosen from a)-p) of the following:

(a) SEQ ID NOs: 147, 148, 149, 136, 137, and 138;

(b) SEQ ID NOs: 228, 229, 230, 217, 218, and 219;

(c) SEQ ID NOs: 66, 67, 68, 55, 56, and 57;

(d) SEQ ID NOs: 93, 94, 95, 82, 83, and 84;

(e) SEQ ID NOs: 120, 121, 122, 109, 110, and 111;

(f) SEQ ID NOs: 12, 13, 14, 1, 2, and 3;

(g) SEQ ID NOs: 174, 175, 176, 163, 164, and 165;

(h) SEQ ID NOs: 201, 202, 203, 190, 191, and 192;

(i) SEQ ID NOs: 39, 40, 41, 28, 29, and 30;

(j) SEQ ID NOs: 255, 256, 257, 244, 245, and 246;

(k) SEQ ID NOs: 282, 283, 284, 271, 272, and 273;

(l) SEQ ID NOs: 309, 310, 311, 298, 299, and 300;

(m) SEQ ID NOs: 336, 337, 338, 325, 326, and 327;

(n) SEQ ID NOs: 363, 364, 365, 352, 353, and 354;

(o) SEQ ID NOs: 390, 391, 392, 379, 380, and 381; and

(p) SEQ ID NOs: 417, 418, 419, 406, 407, and 408.

3. The isolated nucleic acid molecule of claim 1 or 2, wherein:

(i) the CAR comprises any light chain variable region listed in Table 1 or Table 5;

(ii) the CAR comprises any heavy chain variable region listed in Table 1 or Table 4;

(iii) the CAR comprises any light chain variable region listed in Table 1 or Table 5 and any heavy chain variable region listed in Table 1 or Table 4;

(iv) the CAR comprises a light chain variable region and a heavy chain variable region, respectively, chosen from a) to p) of the following:

(a) SEQ ID NOs: 156 and 145;

(b) SEQ ID NOs: 237 and 226;

(c) SEQ ID NOs: 21 and 10

(d) SEQ ID NOs: 75 and 64;

(e) SEQ ID NOs: 102 and 91;

(f) SEQ ID NOs: 129 and 118;

(g) SEQ ID NOs: 183 and 172;

(h) SEQ ID NOs: 210 and 199;

(i) SEQ ID NOs: 48 and 37;

(j) SEQ ID NOs: 264 and 253;

(k) SEQ ID NOs: 291 and 280;

(l) SEQ ID NOs: 318 and 307;

(m) SEQ ID NOs: 345 and 334;

(n) SEQ ID NOs: 372 and 361;

(o) SEQ ID NOs: 399 and 388; and

(p) SEQ ID NOs: 426 and 415;

(v) the CD20 binding domain is a scFv;

(vi) the CAR comprises a light chain variable region comprising an amino acid sequence having at least one, two, or three modifications but not more than 30, 20 or 10 modifications of an amino acid sequence of a light chain variable region provided in Table 1 or Table 5, or an amino acid sequence with at least 95% identity to an amino acid sequence provided in Table 1 or Table 5;

(vii) the CAR comprises a heavy chain variable region comprising an amino acid sequence having at least one, two or three modifications but not more than 30, 20 or 10 modifications of an amino acid sequence of a heavy chain variable region provided in Table 1 or Table 4, or an amino acid sequence with at least 95% identity to an amino acid sequence provided in Table 1 or Table 4;

(viii) the CD20 binding domain comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 159, SEQ ID NO: 240, SEQ ID NO: 24, SEQ ID NO: 51, SEQ ID NO: 78, SEQ ID NO: 105, SEQ ID NO: 132, SEQ ID NO: 186, SEQ ID NO: 213, SEQ ID NO: 267, SEQ ID NO: 294, SEQ ID NO: 321, SEQ ID NO: 348, SEQ ID NO: 375, SEQ ID NO: 402, and SEQ ID NO: 429, or an amino acid sequence with at least 95% identity thereto, or having at least one, two or three modifications but not more than 20, 10 or 5 modifications relative to any of the aforesaid amino acid sequences;

(ix) the nucleic acid sequence encoding the CD20 binding domain comprises a nucleotide sequence selected from the group consisting of SEQ ID NO: 160, SEQ ID NO: 241, SEQ ID NO: 25, SEQ ID NO: 52, SEQ ID NO: 79, SEQ ID NO: 106, SEQ ID NO: 133, SEQ ID NO: 187, SEQ ID NO: 214, SEQ ID NO: 268, SEQ ID NO: 295, SEQ ID NO: 322, SEQ ID NO: 349, SEQ ID NO: 376, SEQ ID NO: 403, and SEQ ID NO: 430, or a nucleotide sequence with at least 95% identity thereto;

(x) the nucleic acid molecule comprises a nucleic acid sequence listed in Table 1;

(xi) the nucleic acid molecule comprises a nucleotide sequence selected from the group consisting of SEQ ID NO: 160, SEQ ID NO: 241, SEQ ID NO: 25, SEQ ID NO: 52, SEQ ID NO: 79, SEQ ID NO: 106, SEQ ID NO: 133, SEQ ID NO: 187, SEQ ID NO: 214, SEQ ID NO: 268, SEQ ID NO: 295, SEQ ID NO: 322, SEQ ID NO: 349, SEQ ID NO: 376, SEQ ID NO: 403, and SEQ ID NO: 430, or a nucleotide sequence with at least 95% identity thereto; or

(xii) the nucleic acid molecule comprises a nucleotide sequence selected from the group consisting of SEQ ID NO: 160, SEQ ID NO: 241, SEQ ID NO: 25, SEQ ID NO: 52, SEQ ID NO: 79, SEQ ID NO: 106, SEQ ID NO: 133, SEQ ID NO: 187, SEQ ID NO: 214, SEQ ID NO: 268, SEQ ID NO: 295, SEQ ID NO: 322, SEQ ID NO: 349, SEQ ID NO: 376, SEQ ID NO: 403, and SEQ ID NO: 430.

4. The isolated nucleic acid molecule of any one of claims 1-3, wherein:

(i) the transmembrane domain comprises a transmembrane domain of a protein selected from the group consisting of the alpha, beta or zeta chain of the T-cell receptor, CD28, CD3 epsilon, CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD123, CD134, CD137 and CD154;

(ii) the transmembrane domain comprises an amino acid sequence comprising at least one, two or three modifications but not more than 20, 10 or 5 modifications of the amino acid sequence of SEQ ID NO: 801, or an amino acid sequence with at least 95% identity to the amino acid sequence of SEQ ID NO: 801;

(iii) the transmembrane domain comprises the amino acid sequence of SEQ ID NO: 801;

(iv) the CD20 binding domain is connected to the transmembrane domain by a hinge region;

(v) the CD20 binding domain is connected to the transmembrane domain by a hinge region, wherein the hinge region comprises the amino acid sequence of SEQ ID NO: 799, or SEQ ID NO: 814, or an amino acid sequence with at least 95% identity thereto; or

(vi) the CD20 binding domain is connected to the transmembrane domain by a hinge region, wherein the nucleic acid sequence encoding the hinge region comprises the nucleotide sequence of SEQ ID NO: 800 or SEQ ID NO: 815, or a nucleotide sequence with at least 95% identity thereto.

5. The isolated nucleic acid molecule of any one of claims 1-4, wherein:

(i) the intracellular signaling domain comprises a costimulatory domain;

(ii) the intracellular signaling domain comprises a costimulatory domain, wherein the costimulatory domain is a functional signaling domain obtained from a protein selected from the group consisting of OX40, CD2, CD27, CD28, CDS, ICAM-1, LFA-1 (CD11a/CD18), ICOS (CD278) and 4-1BB (CD137);

(iii) the intracellular signaling domain comprises a costimulatory domain, wherein the costimulatory domain comprises an amino acid sequence having at least one, two or three modifications but not more than 20, 10 or 5 modifications of the amino acid sequence of SEQ ID NO: 803, or an amino acid sequence with at least 95% identity to the amino acid sequence of SEQ ID NO: 803;

(iv) the intracellular signaling domain comprises a costimulatory domain, wherein the costimulatory domain comprises the amino acid sequence of SEQ ID NO: 803;

(v) the intracellular signaling domain comprises a costimulatory domain, wherein the nucleic acid sequence encoding the costimulatory domain comprises the nucleotide sequence of SEQ ID NO: 804, or a nucleotide sequence with at least 95% identity thereto;

(vi) the intracellular signaling domain comprises a primary signaling domain;

(vii) the intracellular signaling domain comprises a primary signaling domain, wherein the primary signaling domain comprises a functional signaling domain of CD3 zeta;

(viii) the intracellular signaling domain comprises a primary signaling domain, wherein the primary signaling domain comprises the amino acid sequence of SEQ ID NO: 805 or SEQ ID NO: 807;

(ix) the intracellular signaling domain comprises a functional signaling domain of 4-1BB and/or a functional signaling domain of CD3 zeta;

(x) the intracellular signaling domain comprises an amino acid sequence having at least one, two or three modifications but not more than 20, 10 or 5 modifications of the amino acid sequence of SEQ ID NO: 803 and/or the amino acid sequence of SEQ ID NO: 805 or SEQ ID NO: 807, or an amino acid sequence with at least 95% identity to the amino acid sequence of SEQ ID NO: 803 and/or the amino acid sequence of SEQ ID NO: 805 or SEQ ID NO: 807;

(xi) the intracellular signaling domain comprises the amino acid sequence of SEQ ID NO: 803 and/or the amino acid sequence of SEQ ID NO: 805 or SEQ ID NO: 807;

(xii) the intracellular signaling domain comprises the amino acid sequence of SEQ ID NO: 803 and the amino acid sequence of SEQ ID NO: 805 or SEQ ID NO: 807;

(xiii) the intracellular signaling domain comprises the amino acid sequence of SEQ ID NO: 803 and the amino acid sequence of SEQ ID NO: 805 or SEQ ID NO: 807, wherein the sequences comprising the intracellular signaling domain are expressed in the same frame and as a single polypeptide chain; or

(xiv) the nucleic acid sequence encoding the intracellular signaling domain comprises the nucleotide sequence of SEQ ID NO: 804, or a nucleotide sequence with at least 95% identity thereto, and/or the nucleotide sequence of SEQ ID NO: 893, 808, 806, or 1074, or a nucleotide sequence with at least 95% identity thereto.

6. The isolated nucleic acid molecule of any one of claims 1-5, further comprising a leader sequence, optionally wherein the leader sequence encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 797.

7. The isolated nucleic acid molecule of any one of claims 1-6, wherein:
(i) the nucleic acid molecule encodes a CAR comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 161, SEQ ID NO: 242, SEQ ID NO: 26, SEQ ID NO: 53, SEQ ID NO: 80, SEQ ID NO: 107, SEQ ID NO: 134, SEQ ID NO: 188, SEQ ID NO: 215, SEQ ID NO: 269, SEQ ID NO: 296, SEQ ID NO: 323, SEQ ID NO: 350, SEQ ID NO: 377, SEQ ID NO: 404 and SEQ ID NO: 431, or an amino acid sequence with at least 95% identity thereto, or an amino acid sequence comprising at least one, two or three

modifications but not more than 30, 20, 10 or 5 modifications of the amino acid sequence of SEQ ID NO: 161, SEQ ID NO: 242, SEQ ID NO: 26, SEQ ID NO: 53, SEQ ID NO: 80, SEQ ID NO: 107, SEQ ID NO: 134, SEQ ID NO: 188, SEQ ID NO: 215, SEQ ID NO: 269, SEQ ID NO: 296, SEQ ID NO: 323, SEQ ID NO: 350, SEQ ID NO: 377, SEQ ID NO: 404 or SEQ ID NO: 431, optionally wherein the CAR comprises or does not comprise a signal peptide comprising the amino acid sequence of SEQ ID NO: 797;

(ii) the nucleic acid molecule encodes a CAR comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 161, SEQ ID NO: 242, SEQ ID NO: 26, SEQ ID NO: 53, SEQ ID NO: 80, SEQ ID NO: 107, SEQ ID NO: 134, SEQ ID NO: 188, SEQ ID NO: 215, SEQ ID NO: 269, SEQ ID NO: 296, SEQ ID NO: 323, SEQ ID NO: 350, SEQ ID NO: 377, SEQ ID NO: 404 and SEQ ID NO: 431, wherein the CAR comprises or does not comprise a signal peptide comprising the amino acid sequence of SEQ ID NO: 797;

(iii) the nucleic acid molecule comprises a nucleotide sequence selected from the group consisting of SEQ ID NO: 162, SEQ ID NO: 243, SEQ ID NO: 27, SEQ ID NO: 54, SEQ ID NO: 81, SEQ ID NO: 108, SEQ ID NO: 135, SEQ ID NO: 189, SEQ ID NO: 216, SEQ ID NO: 270, SEQ ID NO: 297, SEQ ID NO: 324, SEQ ID NO: 351, SEQ ID NO: 378, SEQ ID NO: 405, and SEQ ID NO: 432, or a nucleotide sequence with at least 95% identity thereto, wherein the nucleic acid molecule comprises or does not comprise the nucleotide sequence of SEQ ID NO: 798; or

(iv) the nucleic acid molecule comprises a nucleotide sequence selected from the group consisting of SEQ ID NO: 162, SEQ ID NO: 243, SEQ ID NO: 27, SEQ ID NO: 54, SEQ ID NO: 81, SEQ ID NO: 108, SEQ ID NO: 135, SEQ ID NO: 189, SEQ ID NO: 216, SEQ ID NO: 270, SEQ ID NO: 297, SEQ ID NO: 324, SEQ ID NO: 351, SEQ ID NO: 378, SEQ ID NO: 405, and SEQ ID NO: 432, wherein the nucleic acid molecule comprises or does not comprise the nucleotide sequence of SEQ ID NO: 798.

8. An isolated polypeptide molecule encoded by the nucleic acid molecule of any one of claims 1-7.

9. An isolated CAR molecule comprising a CD20 binding domain, a transmembrane domain, and an intracellular signaling domain, wherein the CD20 binding domain comprises one or more light chain complementarity determining region 1 (LCDR1), light chain complementarity determining region 2 (LCDR2), and light chain complementarity

determining region 3 (LCDR3) listed in Table 1 or Table 3, and one or more heavy chain complementarity determining region 1 (HCDR1), heavy chain complementarity determining region 2 (HCDR2), and heavy chain complementarity determining region 3 (HCDR3) listed in Table 1 or Table 2.

10. The isolated CAR molecule of claim 9, wherein:

(i) the CAR molecule comprises LCDR1, LCDR2 and LCDR3 of any sequence listed in Table 1 or Table 3;

(ii) the CAR molecule comprises HCDR1, HCDR2, and HCDR3 of any sequence listed in Table 1 or Table 2;

(iii) the CAR molecule comprises LCDR1, LCDR2 and LCDR3 of any sequence listed in Table 1 or Table 3, and HCDR1, HCDR2, and HCDR3 of any sequence listed in Table 1 or Table 2;

(iv) the LCDR1, LCDR2, or LCDR3 comprises an amino acid sequence listed in Table 1; or

(v) the HCDR1, HCDR2, or HCDR3 comprises an amino acid sequence listed in Table 1.

11. The isolated CAR molecule of claim 9 or 10, wherein:

(i) the CAR molecule comprises any light chain variable region listed in Table 1 or Table 5;

(ii) the CAR molecule comprises any heavy chain variable region listed in Table 1 or Table 4;

(iii) the CAR molecule comprises any light chain variable region listed in Table 1 or Table 5 and any heavy chain variable region listed in Table 1 or Table 4;

(iv) the CD20 binding domain is an scFv;

(v) the CD20 binding domain comprises a light chain variable region and a heavy chain variable region of an amino acid sequence listed in Table 1;

(vi) the CD20 binding domain comprises: a light chain variable region comprising an amino acid sequence having at least one, two or three modifications but not more than 30, 20 or 10 modifications of an amino acid sequence of a light chain variable region provided in Table 1 or Table 5, or an amino acid sequence with at least 95% identity to an amino acid sequence provided in Table 1 or Table 5;

(vii) the CD20 binding domain comprises a heavy chain variable region comprising an amino acid sequence having at least one, two or three modifications but not more than 30, 20 or 10 modifications of an amino acid sequence of a heavy chain variable region provided in Table 1 or Table 4, or an amino acid sequence with at least 95% identity to an amino acid sequence provided in Table 1 or Table 4; or

(viii) the CD20 binding domain comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 159, SEQ ID NO: 240, SEQ ID NO: 24, SEQ ID NO: 51, SEQ ID NO: 78, SEQ ID NO: 105, SEQ ID NO: 132, SEQ ID NO: 186, SEQ ID NO: 213, SEQ ID NO: 267, SEQ ID NO: 294, SEQ ID NO: 321, SEQ ID NO: 348, SEQ ID NO: 375, SEQ ID NO: 402, and SEQ ID NO: 429, or an amino acid sequence with at least 95% identity thereto.

12. The isolated CAR molecule of any one of claims 9-11, wherein:

(i) the CAR molecule comprises a transmembrane domain of a protein selected from the group consisting of the alpha, beta or zeta chain of the T-cell receptor, CD28, CD3 epsilon, CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD123, CD134, CD137 and CD154;

(ii) the transmembrane domain comprises an amino acid sequence having at least one, two or three modifications but not more than 20, 10 or 5 modifications of the amino acid sequence of SEQ ID NO: 801, or an amino acid sequence with at least 95% identity to the amino acid sequence of SEQ ID NO: 801;

(iii) the transmembrane domain comprises the amino acid sequence of SEQ ID NO: 801;

(iv) the CD20 binding domain is connected to the transmembrane domain by a hinge region, optionally wherein the hinge region comprises the amino acid sequence of SEQ ID NO: 799, or SEQ ID NO: 814, or an amino acid sequence with at least 95% identity thereto.

13. The isolated CAR molecule of any one of claims 9-12, wherein:

(i) the intracellular signaling domain comprises a costimulatory domain;

(ii) the intracellular signaling domain comprises a costimulatory domain, wherein the costimulatory domain comprises a functional signaling domain of a protein selected from the

group consisting of OX40, CD2, CD27, CD28, CDS, ICAM-1, LFA-1 (CD11a/CD18), ICOS (CD278) and 4-1BB (CD137);

(iii) the intracellular signaling domain comprises a costimulatory domain, wherein the costimulatory domain comprises an amino acid sequence having at least one, two or three modifications but not more than 20, 10 or 5 modifications of the amino acid sequence of SEQ ID NO: 803, or an amino acid sequence with at least 95% identity to the amino acid sequence of SEQ ID NO: 803;

(iv) the intracellular signaling domain comprises a costimulatory domain, wherein the costimulatory domain comprises the amino acid sequence of SEQ ID NO: 803;

(v) the intracellular signaling domain comprises a primary signaling domain;

(vi) the intracellular signaling domain comprises a primary signaling domain, wherein the primary signaling domain comprises a functional signaling domain of CD3 zeta;

(vii) the intracellular signaling domain comprises a primary signaling domain, wherein the primary signaling domain comprises the amino acid sequence of SEQ ID NO: 805 or SEQ ID NO: 807;

(viii) the intracellular signaling domain comprises a functional signaling domain of 4-1BB and/or a functional signaling domain of CD3 zeta;

(ix) the intracellular signaling domain comprises the amino acid sequence of SEQ ID NO: 803 and/or the amino acid sequence of SEQ ID NO: 805;

(x) the intracellular signaling domain comprises the amino acid sequence of SEQ ID NO:803 and/or the amino acid sequence of SEQ ID NO:807;

(xi) the intracellular signaling domain comprises an amino acid sequence having at least one, two or three modifications but not more than 20, 10 or 5 modifications of the amino acid sequence of SEQ ID NO:803 and/or the amino acid sequence of SEQ ID NO: 805 or SEQ ID NO: 807, or an amino acid sequence with at least 95% identity to the amino acid sequence of SEQ ID NO: 803 and/or the amino acid sequence of SEQ ID NO: 805 or SEQ ID NO: 807; or

(xii) the intracellular signaling domain comprises the amino acid sequence of SEQ ID NO: 803 and the amino acid sequence of SEQ ID NO: 805 or SEQ ID NO: 807, wherein the sequences comprising the intracellular signaling domain are expressed in the same frame and as a single polypeptide chain.

14. The isolated CAR molecule of any one of claims 9-13, further comprising a leader sequence, optionally wherein the leader sequence comprises the amino acid sequence of SEQ ID NO: 797, or an amino acid sequence with at least 95% identity to the amino acid sequence of SEQ ID NO: 797.

15. The isolated CAR molecule of any one of claims 9-14, comprising:
(i) an amino acid sequence selected from the group consisting of SEQ ID NO: 161, SEQ ID NO: 242, SEQ ID NO: 26, SEQ ID NO: 53, SEQ ID NO: 80, SEQ ID NO: 107, SEQ ID NO: 134, SEQ ID NO: 188, SEQ ID NO: 215, SEQ ID NO: 269, SEQ ID NO: 296, SEQ ID NO: 323, SEQ ID NO: 350, SEQ ID NO: 377, SEQ ID NO: 404, and SEQ ID NO: 431, or an amino acid sequence with at least 95% identity thereto or an amino acid sequence comprising at least one, two or three modifications but not more than 30, 20, 10 or 5 modifications of the amino acid sequence of SEQ ID NO: 161, SEQ ID NO: 242, SEQ ID NO: 26, SEQ ID NO: 53, SEQ ID NO: 80, SEQ ID NO: 107, SEQ ID NO: 134, SEQ ID NO: 188, SEQ ID NO: 215, SEQ ID NO: 269, SEQ ID NO: 296, SEQ ID NO: 323, SEQ ID NO: 350, SEQ ID NO: 377, SEQ ID NO: 404, or SEQ ID NO: 431, wherein the CAR molecule comprises or does not comprise a signal peptide comprising the amino acid sequence of SEQ ID NO: 797; or
(ii) an amino acid sequence selected from the group consisting of SEQ ID NO: 161, SEQ ID NO: 242, SEQ ID NO: 26, SEQ ID NO: 53, SEQ ID NO: 80, SEQ ID NO: 107, SEQ ID NO: 134, SEQ ID NO: 188, SEQ ID NO: 215, SEQ ID NO: 269, SEQ ID NO: 296, SEQ ID NO: 323, SEQ ID NO: 350, SEQ ID NO: 377, SEQ ID NO: 404 and SEQ ID NO: 431, wherein the CAR molecule comprises or does not comprise a signal peptide comprising the amino acid sequence of SEQ ID NO: 797.

16. A CD20 binding domain comprising one or more light chain complementarity determining region 1 (LCDR1), light chain complementarity determining region 2 (LCDR2), and light chain complementarity determining region 3 (LCDR3) of any CD20 binding domain selected from the group consisting of SEQ ID NO: 159, SEQ ID NO: 240, SEQ ID NO: 24, SEQ ID NO: 51, SEQ ID NO: 78, SEQ ID NO: 105, SEQ ID NO: 132, SEQ ID NO: 186, SEQ ID NO: 213, SEQ ID NO: 267, SEQ ID NO: 294, SEQ ID NO: 321, SEQ ID NO: 348, SEQ ID NO: 375, SEQ ID NO: 402, and SEQ ID NO: 429, and one or more heavy chain

complementarity determining region 1 (HCDR1), heavy chain complementarity determining region 2 (HCDR2), and heavy chain complementarity determining region 3 (HCDR3) of any CD20 binding domain selected from the group consisting of SEQ ID NO: 159, SEQ ID NO: 240, SEQ ID NO: 24, SEQ ID NO: 51, SEQ ID NO: 78, SEQ ID NO: 105, SEQ ID NO: 132, SEQ ID NO: 186, SEQ ID NO: 213, SEQ ID NO: 267, SEQ ID NO: 294, SEQ ID NO: 321, SEQ ID NO: 348, SEQ ID NO: 375, SEQ ID NO: 402, and SEQ ID NO: 429.

17. The CD20 binding domain of claim 16, wherein:

(i) the LCDR1, LCDR2, and/or LCDR3 comprises an amino acid sequence chosen from Table 1 or Table 3;

(ii) the amino acid sequence of the LCDR1, LCDR2, and LCDR3, respectively, is chosen from a)-p) of the following:

(a) SEQ ID NOs: 147, 148, and 149;

(b) SEQ ID NOs: 228, 229, and 230;

(c) SEQ ID NOs: 66, 67, and 68;

(d) SEQ ID NOs: 93, 94, and 95;

(e) SEQ ID NOs: 120, 121, and 122;

(f) SEQ ID NOs: 12, 13, and 14;

(g) SEQ ID NOs: 174, 175, and 176;

(h) SEQ ID NOs: 201, 202, and 203;

(i) SEQ ID NOs: 39, 40, and 41;

(j) SEQ ID NOs: 255, 256, and 257;

(k) SEQ ID NOs: 282, 283, and 284;

(l) SEQ ID NOs: 309, 310, and 311;

(m) SEQ ID NOs: 336, 337, and 338;

(n) SEQ ID NOs: 363, 364, and 365;

(o) SEQ ID NOs: 390, 391, and 392; and

(p) SEQ ID NOs: 417, 418, and 419;

(iii) the HCDR1, HCDR2, and/or HCDR3 comprises an amino acid sequence chosen from Table 1 or Table 2;

(iv) the amino acid sequence of the HCDR1, HCDR2, and HCDR3, respectively, is chosen from a)-p) of the following:

(a) SEQ ID NOs: 136, 137, and 138;

(b) SEQ ID NOs: 217, 218, and 219;

(c) SEQ ID NOs: 55, 56, and 57;

(d) SEQ ID NOs: 82, 83, and 84;

(e) SEQ ID NOs: 109, 110, and 111;

(f) SEQ ID NOs: 1, 2, and 3;

(g) SEQ ID NOs: 163, 164, and 165;

(h) SEQ ID NOs: 190, 191, and 192;

(i)SEQ ID NOs: 28, 29, and 30;

(j) SEQ ID NOs: 244, 245, and 246;

(k) SEQ ID NOs: 271, 272, and 273;

(l) SEQ ID NOs: 298, 299, and 300;

(m) SEQ ID NOs: 325, 326, and 327;

(n) SEQ ID NOs: 352, 353, and 354;

(o) SEQ ID NOs: 379, 380, and 381; and

(p) SEQ ID NOs: 406, 407, and 408; or

(v) the amino acid sequence of the LCDR1, LCDR2, LCDR3, HCDR1, HCDR2, and HCDR3, respectively, is chosen from a)-p) of the following:

(a) SEQ ID NOs: 147, 148, 149, 136, 137, and 138;

(b) SEQ ID NOs: 228, 229, 230, 217, 218, and 219;

(c) SEQ ID NOs: 66, 67, 68, 55, 56, and 57;

(d) SEQ ID NOs: 93, 94, 95, 82, 83, and 84;

(e) SEQ ID NOs: 120, 121, 122, 109, 110, and 111;

(f) SEQ ID NOs: 12, 13, 14, 1, 2, and 3;

(g) SEQ ID NOs: 174, 175, 176, 163, 164, and 165;

(h) SEQ ID NOs: 201, 202, 203, 190, 191, and 192;

(i) SEQ ID NOs: 39, 40, 41, 28, 29, and 30;

(j) SEQ ID NOs: 255, 256, 257, 244, 245, and 246;

(k) SEQ ID NOs: 282, 283, 284, 271, 272, and 273;

(l) SEQ ID NOs: 309, 310, 311, 298, 299, and 300;

(m) SEQ ID NOs: 336, 337, 338, 325, 326, and 327;

(n) SEQ ID NOs: 363, 364, 365, 352, 353, and 354;

(o) SEQ ID NOs: 390, 391, 392, 379, 380, and 381; and

(p) SEQ ID NOs: 417, 418, 419, 406, 407, and 408.

18. The CD20 binding domain of claim 16 or 17, wherein:

(i) the CD20 binding domain is a scFv comprising a light chain variable region of an amino acid sequence selected from Table 1 or Table 5 and a heavy chain variable region of an amino acid sequence selected from Table 1 or Table 4;

(ii) the CD20 binding domain comprises a light chain variable region and a heavy chain variable region, wherein the amino acid sequence of the light chain variable region and the heavy chain variable region, respectively, is chosen from a) to p) of the following:

(a) SEQ ID NOs: 156 and 145;

(b) SEQ ID NOs: 237 and 226;

(c) SEQ ID NOs: 21 and 10

(d) SEQ ID NOs: 75 and 64;

(e) SEQ ID NOs: 102 and 91;

(f) SEQ ID NOs: 129 and 118;

(g) SEQ ID NOs: 183 and 172;

(h) SEQ ID NOs: 210 and 199;

(i) SEQ ID NOs: 48 and 37;

(j) SEQ ID NOs: 264 and 253;

(k) SEQ ID NOs: 291 and 280;

(l) SEQ ID NOs: 318 and 307;

(m) SEQ ID NOs: 345 and 334;

(n) SEQ ID NOs: 372 and 361;

(o) SEQ ID NOs: 399 and 388; and

(p) SEQ ID NOs: 426 and 415; or

(iii) the CD20 binding domain comprises: a light chain variable region comprising an amino acid sequence having at least one, two or three modifications but not more than 30, 20 or 10 modifications of an amino acid sequence of a light chain variable region provided in Table 1 or Table 5, or an amino acid sequence with at least 95% identity to an amino acid sequence in Table 1 or Table 5; and/or a heavy chain variable region comprising an amino acid sequence having at least one, two or three modifications but not more than 30, 20 or 10 modifications of an amino acid sequence of a heavy chain variable region provided in Table 1 or Table 4, or an amino acid sequence with at least 95% identity to an amino acid sequence in Table 1 or Table 4.

19. A nucleic acid molecule encoding:
(i) a first nucleic acid molecule encoding the CAR molecule of any one of claims 9-15, and
(ii) a second nucleic acid molecule encoding a CAR molecule that binds a B-cell antigen, e.g., CD19, CD22, CD10, CD34, CD123, FLT-3, ROR-1, CD79b, CD79a, or CD179b, e.g., wherein the first and the second nucleic acid molecules are disposed on a single nucleic acid molecule or the first and the second nucleic acid molecules are disposed on separate nucleic acid molecules.

20. The nucleic acid molecule of claim 19, wherein:

(i) the B-cell antigen is CD19 or CD22;

(ii) the CAR molecule that binds to a B-cell antigen binds to CD19 and comprises a nucleotide sequence encoding a CD19 CAR according to Table 11, e.g., CTL-019 or humanized CAR2; or

(iii) the CAR molecule that binds to a B-cell antigen binds to CD22 and comprises a nucleotide sequence encoding a CD22 CAR according to Table 6, e.g., CD22-65 CAR, CD22-65KD CAR, CD22-65s CAR or CD22-65ss CAR.

21. The nucleic acid molecule of claim 19 or 20, wherein:

(i) a nucleotide sequence encoding a cleavable peptide, e.g., a P2A or F2A, or a nucleotide sequence encoding an IRES is disposed between the first nucleic acid molecule and the second nucleic acid molecule;

(ii) the first nucleic acid molecule and the second nucleic acid molecule comprise a single promoter, e.g., as a bicistronic transcription product;

(iii) the first nucleic acid molecule and the second nucleic acid molecule comprise a single promoter, wherein the single promoter is an EF-1α promoter, optionally wherein the EF-1α promoter comprises the nucleotide sequence of SEQ ID NO: 833;

(iv) the first nucleic acid molecule comprises a first promoter and the second nucleic acid molecule comprises a second promoter; or

(v) the nucleic acid molecule comprises RNA or DNA.

22. An isolated polypeptide molecule encoded by the nucleic acid molecule of any one of claims 19-21.

23. A CD22 binding domain, or a CAR molecule, comprising:

(i) a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 839; and/or

(ii) a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 840.

24. The CD22 binding domain or CAR molecule of claim 23, wherein:

(i) the VH and VL sequences are connected directly, e.g., without a linker;
(ii) the VH and VL sequences are connected via a linker comprising the amino acid sequence of SEQ ID NO: 1089, optionally wherein the linker comprises the amino acid sequence of SEQ ID NO: 1083; or
(iii) the CD22 binding domain or CAR molecule comprises the amino acid sequence of SEQ ID NO: 837.

25. A CD22 binding domain, or a CAR molecule, comprising the amino acid sequence of SEQ ID NO: 835 or SEQ ID NO: 836.

26. A nucleic acid molecule encoding the CD22 binding domain or the CAR molecule of any one of claims 23-25.

27. A multispecific, e.g., bispecific, antibody molecule, or CAR molecule, having a first binding specificity for CD20 and a second binding specificity for one or more of CD19, CD22, CD10, CD34, CD123, FLT-3, ROR1, CD79b, CD179b, or CD79a, wherein the first binding specificity comprises the CD20 binding domain of any one of claims 16-18.

28. A multispecific, e.g., bispecific, antibody molecule, or CAR molecule, having a first binding specificity for CD22 and a second binding specificity for one or more of CD19, CD20, CD10, CD34, CD123, FLT-3, ROR1, CD79b, CD179b, or CD79a, wherein the first binding specificity comprises the CD22 binding domain of any one of claims 23-25.

29. A multispecific, e.g., bispecific, antibody molecule, or CAR molecule, having a first binding specificity for CD19 and a second binding specificity for one or both of CD20 or CD22, wherein:

(i) the multispecific, e.g., bispecific antibody molecule has the arrangement VH_1-VL_1-VL_2-VH_2, from an N- to C-terminal orientation;

(ii) the multispecific, e.g., bispecific antibody molecule has the arrangement VL_1-VH_1-VH_2-VL_2, from an N- to C-terminal orientation;

(iii) the multispecific, e.g., bispecific antibody molecule has the arrangement VL_1-VH_1-VL_2-VH_2, from an N- to C-terminal orientation; or

(iv) the multispecific, e.g., bispecific antibody molecule has the arrangement VH_1-VL_1-VH_2-VL_2, from an N- to C-terminal orientation, and

wherein a linker is disposed between the two antibodies or antibody fragments (e.g., scFvs), e.g., between VL_1 and VL_2 if the construct is arranged as VH_1-VL_1-VL_2-VH_2; between VH_1 and VH_2 if the construct is arranged as VL_1-VH_1-VH_2-VL_2; between VH_1 and VL_2 if the construct is arranged as VL_1-VH_1-VL_2-VH_2; or between VL_1 and VH_2 if the construct is arranged as VH_1-VL_1-VH_2-VL_2.

30. The multispecific antibody molecule, or CAR molecule, of claim 29, wherein:
(i) the second binding specificity is for CD20, wherein the CD20 binding specificity comprises a VH and VL as depicted in Table 1, e.g., a VH and VL from a CD20-C3H2 or CD20-C5H1;
(ii) the second binding specificity is for CD22, wherein the CD22 binding specificity comprises a VH and VL as depicted in Table 6, e.g., a VH and VL from a CD22-65, e.g., a CD22-65ss scFv, CD22-65s scFv, or CD22-65KD scFv;
(iii) the linker comprises the amino acid sequence of SEQ ID NO: 1089, or the linker comprises, or consists of, the amino acid sequence of SEQ ID NO: 1091;
(iv) the CD19 binding specificity comprises a VH and VL as depicted in Table 11, e.g., a CTL019 scFv (SEQ ID NO: 765), e.g., a humanized CD19 scFv, e.g., a humanized CAR2;
(v) the multispecific antibody molecule, or CAR molecule comprises a VL1-VH1 binding specificity to CD19, and a VL2-VH2 or VH2-VL2 binding specificity to CD22;
(vi) the multispecific antibody molecule, or CAR molecule is encoded by a nucleic acid molecule comprising, or consisting of, the nucleotide sequence of any of SEQ ID NOs: 844, 846, 848, 850, 852, 854, 856, 860, 895, 859, 861, 863, 865, 867, 869, 871, or 873, or a nucleotide sequence at least 95% identical to any of the aforesaid sequences; or
(vii) the multispecific antibody molecule, or CAR molecule comprises, or consists of, the amino acid sequence of any of SEQ ID NOs: 845, 847, 849, 851, 853, 855, 857, 858, 860, 862, 864, 866, 868, 870, 872, or 874, or an amino acid sequence at least 95% identical to any of the aforesaid sequences or having at least one, two or three modifications but not more than 30, 20 or 10 modifications.

31. The multispecific antibody molecule, or CAR molecule, of any one of claim 27-30, wherein the multispecific antibody molecule is present in a CAR molecule, wherein:
(i) the CAR molecule comprises a proximal or distal binding specificity for CD19;
(ii) the CAR molecule comprises a proximal or distal binding specificity for CD22; or
(iii) the CAR molecule comprises a proximal or distal binding specificity for CD20.

32. A nucleic acid molecule encoding the multispecific antibody molecule or the CAR molecule of any one of claims 27-31.

33. A nucleic acid molecule encoding a multispecific antibody molecule or a CAR molecule, comprising, or consisting of, the nucleotide sequence of any of SEQ ID NOs: 844, 846, 848, 850, 852, 854, 856, 860, 895, 859, 861, 863, 865, 867, 869, 871, or 873, or a nucleotide sequence at least 95% identical to any of the aforesaid sequences.

34. A vector, e.g., a one or both of a first and a second vector, comprising the nucleic acid molecule of any one of claims 1-7, 19-21, 26, 32, or 33, a nucleic acid molecule encoding the polypeptide molecule of claim 8 or 22, a nucleic acid molecule encoding the CAR molecule of any one of claims 9-15, a nucleic acid molecule encoding the CD20 binding domain of any one of claims 16-18, a nucleic acid molecule encoding the CD22 binding domain or CAR molecule of any one of claims 23-25, or a nucleic acid molecule encoding the multispecific antibody molecule or CAR molecule of any one of claims 27-31, optionally wherein the vector is selected from the group consisting of a DNA, a RNA, a plasmid, a lentivirus vector, an adenoviral vector, or a retrovirus vector.

35. A cell, e.g., a population of immune effector cells (e.g., a first and/or second population of immune effector cells), comprising the nucleic acid molecule of any one of claims 1-7, 19-21, 26, 32, or 33, the polypeptide molecule of claim 8 or 22, the CAR molecule of any one of claims 9-15, the CD20 binding domain of any one of claims 16-18, the CD22 binding domain or CAR molecule of any one of claims 23-25, the multispecific antibody molecule of any one of claims 27-31, or the vector of claim 34.

36. A method of making a cell, e.g., a population of immune effector cells, comprising transducing a T cell or an NK cell with the nucleic acid molecule of any one of claims 1-7, 19-21, 26, 32, or 33 or the vector of claim 34.

37. A method of generating a population of RNA-engineered cells comprising introducing an in vitro transcribed RNA or synthetic RNA into a cell, wherein the RNA comprises the nucleic acid molecule of any one of claims 1-7, 19-21, 26, 32, or 33.

38. A population of immune effector cells, comprising:

(i) a first cell population comprising the nucleic acid molecule of any one of claims 1-7, 19-21, 26, 32, or 33, the polypeptide molecule of claim 8 or 22, the CAR molecule of any one of claims 9-15, the CD20 binding domain of any one of claims 16-18, or the vector of claim 34;

and

(ii) a second cell population comprising a nucleic acid molecule encoding a CAR that binds a B-cell antigen, e.g., CD19, CD22, CD10, CD34, CD123, FLT-3, ROR-1, CD79b, CD79a, or CD179b.

39. The population of claim 38, wherein:

(i) the B-cell antigen is CD19 or CD22;

(ii) the CAR that binds a B-cell antigen binds CD19 and comprises a nucleotide sequence encoding a CD19 CAR according to Table 11, e.g., CTL-019 or humanized CAR2; or

(iii) the CAR that binds a B-cell antigen binds CD22 and comprises a nucleotide sequence encoding a CD22 CAR according to Table 6, e.g., CD22-65 CAR, CD22-65KD CAR, CD22-65s CAR or CD22-65ss CAR.

40. Use of a cell, e.g., a population of immune effector cells, expressing the nucleic acid molecule of any one of claims 1-7, 19-21, 26, 32, or 33, the polypeptide molecule of claim 8 or 22, the CAR molecule of any one of claims 9-15, the CD20 binding domain of any one of claims 16-18, the CD22 binding domain or CAR molecule of any one of claims 23-25, the multispecific antibody molecule of any one of claims 27-31, or the vector of any one of claims 23-25, in the manufacture of a medicament for the treatment of a cancer or a disease associated with expression of CD20, CD19, or CD22 in a subject, wherein said use comprises an effective amount of the cell to be administered to the subject.

41. The use of claim 40, wherein:

(i) the disease is acute myeloid leukemia (AML), B-cell acute lymphoid leukemia (BALL), small lymphocytic leukemia (SLL), acute lymphoid leukemia (ALL), chronic myelogenous leukemia (CML), chronic lymphocytic leukemia (CLL), mantle cell lymphoma (MCL), B cell prolymphocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B cell lymphoma (DLBCL), follicular lymphoma, hairy cell leukemia, small cell-lymphoma, large cell-follicular lymphoma, a malignant lymphoproliferative condition, MALT lymphoma, Marginal zone lymphoma, multiple myeloma, myelodysplasia, or myelodysplastic syndrome, myeloproliferative neoplasm, non-Hodgkin’s lymphoma, Hodgkin’s lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenstrom macroglobulinemia, preleukemia, or a combination thereof;

(ii) the disease is lymphoma, e.g., diffuse large B cell lymphoma (DLBCL); or

(iii) the disease is a B-cell malignancy.

42. The use of claim 40 or 41, further comprising a B-cell inhibitor to be administered to the subject, the B-cell inhibitor chosen from one or more of an inhibitor of CD19, CD22, CD10, CD34, CD123, FLT-3, ROR-1, CD79b, CD79a, or CD179b, optionally wherein:
(i) the B-cell inhibitor is a small molecule inhibitor;
(ii) the B-cell inhibitor is a polypeptide, optionally a soluble ligand, an antibody, or antigen-binding fragment thereof that binds to one or more of CD10, CD19, CD22, CD34, CD123, FLT-3, ROR1, CD79b, CD179b, or CD79a;
(iii) the B-cell inhibitor is an inhibitory nucleic acid, optionally a dsRNA, siRNA, or shRNA;
(iv) the B-cell inhibitor is a cell, e.g., a population of immune effector cells, expressing a CAR that binds a B-cell antigen, e.g., CD19, CD22, CD10, CD34, CD123, FLT-3, ROR-1, CD79b, CD79a, or CD179b;
(v) the B-cell inhibitor is to be administered prior to the cell, e.g., a population of immune effector cells expressing a CAR molecule;

(vi) the B-cell inhibitor is to be administered concurrently with the cell, e.g., a population of immune effector cells, expressing a CAR molecule; or

(vii) the B-cell inhibitor is to be administered after the cell, e.g., a population of immune effector cells, expressing a CAR molecule.

43. The use of any one of claims 40-42, wherein the cell is to be administered in combination with:

(i) an agent that increases the efficacy of the cell;

(ii) an agent that ameliorates one or more side effects associated with administration of the cell; or

(iii) an agent that treats the disease associated with CD20.

44. The cell or population of cells of any one of claims 35, 38, or 39, further expressing an inhibitory molecule that comprises a first polypeptide that comprises at least a portion of an inhibitory molecule, associated with a second polypeptide that comprises a positive signal from an intracellular signaling domain, optionally wherein the inhibitory molecule comprises a first polypeptide that comprises at least a portion of PD1 and a second polypeptide comprising a costimulatory domain and primary signaling domain.

45. An inhibitor of CD20 for use in a method of treating a patient who is a non-responder, partial responder, or relapser to a CD19 inhibitor, e.g., a CD19 CAR therapy, comprising the inhibitor of CD20 to be administered to the patient, wherein the inhibitor of CD20 is encoded by the nucleic acid molecule of any one of claims 1-7, 19-21, 26, 32, or 33.