CLAIMS

1. An isolated nucleic acid molecule encoding a chimeric antigen receptor (CAR), wherein the CAR comprises a human anti-CLL-1 binding domain, a transmembrane domain, and an intracellular signaling domain, and wherein said anti-CLL-1 binding domain comprises a heavy chain complementary determining region 1 (HC CDR1), a heavy chain complementary determining region 2 (HC CDR2), and a heavy chain complementary determining region 3 (HC CDR3) of any CLL-1 heavy chain binding domain amino acid sequences listed in Table 2.

2. The isolated nucleic acid molecule of claim 1, wherein said anti-CLL-1 binding domain further comprises a light chain complementary determining region 1 (LC CDR1), a light chain complementary determining region 2 (LC CDR2), and a light chain complementary determining region 3 (LC CDR3) of any anti-CLL-1 light chain binding domain amino acid sequences listed in Table 2.

3. The isolated nucleic acid molecule of claim 2, wherein said LC CDR1, LC CDR2, and LC CDR3 are the LC CDR sequences listed in Table 6, 8, or 4.

4. The isolated nucleic acid molecules of any of claims 1-3, wherein said HC CDR1, HC CDR2, and HC CDR3 are the HC CDR sequences listed in Table 5, 7, or 2.

5. The isolated nucleic acid molecule of any of claims 1-4, which encodes a CAR comprising:

(i) the amino acid sequence of any light chain variable region listed in Table 2;

(ii) an amino acid sequence having at least one, two or three modifications but not more than 30, 20 or 10 modifications of the amino acid sequence of any of the light chain variable regions provided in Table 2; or

(iii) an amino acid sequence with 95-99% identity to the amino acid sequence of any of the light chain variable regions provided in Table 2.

6. The isolated nucleic acid molecule of any of claims 1-5, which encodes a CAR comprising:

(i) the amino acid sequence of any heavy chain variable region listed in Table 2;

(ii) an amino acid sequence having at least one, two or three modifications but not more than 30, 20 or 10 modifications of the amino acid sequence of any of the heavy chain variable regions provided in Table 2: or

(iii) an amino acid sequence with 95-99% identity to the amino acid sequence of any of the heavy chain variable regions provided in Table 2.

7. The isolated nucleic acid molecule of any of claims 1-6, which encodes a CAR comprising the amino acid sequence of any light chain variable region listed in Table 2, and the amino acid sequence of any heavy chain variable region listed Table 2.

8. The isolated nucleic acid molecule of any of the preceding claims, wherein the encoded CLL-1 binding domain comprises:

(i) the amino acid sequence selected from a group consisting of SEQ ID NO:47, 44, 48, 49, 50, 39, 40, 41, 42, 43, 45, 46, 51, 73, 70, 74, 75, 76, 65, 66, 67, 68, 69, 71, 72, 77, 195, 86, 83, 87, 88, 89, 78, 79, 80, 81, 82, 84, 85, 90, or 196;

(ii) an amino acid sequence having at least one, two or three modifications but not more than 30, 20 or 10 modifications to any of SEQ ID NO: 47, 44, 48, 49, 50, 39, 40, 41, 42, 43, 45, 46, 51, 73, 70, 74, 75, 76, 65, 66, 67, 68, 69, 71, 72, 77, 195, 86, 83, 87, 88, 89, 78, 79, 80, 81, 82, 84, 85, 90, or 196; or

(iii) an amino acid sequence with 95-99% identity to any of SEQ ID NO: 47, 44, 48, 49, 50, 39, 40, 41, 42, 43, 45, 46, 51, 73, 70, 74, 75, 76, 65, 66, 67, 68, 69, 71, 72, 77, 195, 86, 83, 87, 88, 89, 78, 79, 80, 81, 82, 84, 85, 90, or 196.

9. The isolated nucleic acid molecule of any of the preceding claims, wherein the CLL-1 binding domain comprises a nucleotide sequence selected from a group consisting of SEQ ID NO: 60, 44, 61, 62, or 63, or a sequence with 95-99% identity thereof.

10. The isolated nucleic acid molecule of any of the preceding claims, wherein the encoded CAR includes a transmembrane domain that 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, CD134, CD137 and CD154.

11. The isolated nucleic acid molecule of any of the preceding claims, wherein:

(i) the encoded transmembrane domain comprises the amino acid sequence of SEQ ID NO: 6, an amino acid sequence comprises 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:6, or a sequence with 95-99% identity to the amino acid sequence of SEQ ID NO:6;

(ii) the nucleic acid sequence encoding the transmembrane domain comprises a sequence of SEQ ID NO:17, or a sequence with 95-99% identity thereof; or

(iii) the nucleic acid sequence encoding the transmembrane domain comprises a sequence encoding a transmembrane domain provided in any of SEQ ID NOs: 104-116 or 198.

12. The isolated nucleic acid molecule of any of the preceding claims, wherein the encoded CLL-1 binding domain is connected to the transmembrane domain by a hinge region.

13. The nucleic acid molecule of claim 12, wherein:

(i) the encoded hinge region comprises the amino acid sequence of SEQ ID NO:2, or a sequence with 95-99% identity thereof;

(ii) the nucleic acid sequence encoding the hinge region comprises the nucleotide sequence of SEQ ID NO: 13, or a sequence with 95-99% identity thereof; or

(iii) the nucleic acid sequence encoding the hinge region comprises a sequence encoding a hinge region provided in any of SEQ ID NOs: 104-116 or 198.

14. The isolated nucleic acid molecule of any of the preceding claims, wherein the encoded costimulatory domain is a functional signaling domain obtained from a protein selected from the group consisting of a MHC class I molecule, TNF receptor proteins, Immunoglobulin-like proteins, cytokine receptors, integrins, signaling lymphocytic activation molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, OX40, CD2, CD7, CD27, CD28, CD30, CD40, CDS, ICAM-1, LFA-1 (CD11a/CD18), 4-1BB (CD137), B7-H3, CDS, ICAM-1, ICOS (CD278), GITR, BAFFR, LIGHT, HVEM

(LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL2R beta, IL2R gamma, IL7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, NKG2C, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, and a ligand that specifically binds with CD83.

15. The isolated nucleic acid molecule of claim 14, wherein the encoded costimulatory domain comprises the amino acid sequence of SEQ ID NO:7, or 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:7, or a sequence with 95-99% identity to the amino acid sequence of SEQ ID NO:7.

16. The isolated nucleic acid molecule of claim 14, wherein the nucleic acid sequence encoding the costimulatory domain comprises the nucleotide sequence of SEQ ID NO:18, or a sequence with 95-99% identity thereof, or the nucleic acid sequence encoding the costimulatory domain comprises a sequence encoding a 4-1BB domain provided in any of SEQ ID NOs: 104-116 or 198, or a sequence with 95-99% identity thereof.

17. The isolated nucleic acid molecule of any of the preceding claims, wherein the encoded intracellular signaling domain comprises a functional signaling domain of 4-1BB and/or a functional signaling domain of CD3 zeta.

18. The isolated nucleic acid molecule of any of the preceding claims, wherein the encoded intracellular signaling domain comprises the amino acid sequence of SEQ ID NO: 7 and/or the sequence of SEQ ID NO:9 or SEQ ID NO:10; or 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:7 and/or the amino acid sequence of SEQ ID NO:9 or SEQ ID NO:10; or a sequence with 95-99% identity to the amino acid sequence of SEQ ID NO:7 and/or the amino acid sequence of SEQ ID NO:9 or SEQ ID NO:10.

19. The isolated nucleic acid molecule of any of the preceding claims, wherein the encoded intracellular signaling domain comprises the sequence of SEQ ID NO:7 and the sequence of SEQ ID NO:9 or SEQ ID NO:10, wherein the sequences comprising the intracellular signaling domain are expressed in the same frame and as a single polypeptide chain.

20. The isolated nucleic acid molecule of any of the preceding claims, wherein the nucleic acid sequence encoding the intracellular signaling domain comprises the sequence of SEQ ID NO:18, or a sequence with 95-99% identity thereof, and/or

(i) the sequence of SEQ ID NO:20 or SEQ ID NO:21, or a sequence with 95-99% identity thereof, or

(ii) the sequence encoding a CD3zeta domain provided in any of SEQ ID NOs: 104-116 or 198, or a sequence with 95-99% identity thereof.

21. The isolated nucleic acid molecule of any of the preceding claims, further comprising a leader sequence which encodes the amino acid sequence of SEQ ID NO:1.

22. The isolated nucleic acid molecule of any of the preceding claims, which encodes a CAR comprising:

(i) the amino acid sequence of any of SEQ ID NOs:99, 96, 100, 101, 102, 91, 92, 93, 94, 95, 97, 98, 103, or 197;

(ii) an amino acid sequence having at least one, two or three modifications but not more than 30, 20 or 10 modifications to any of SEQ ID NOs: 99, 96, 100, 101, 102, 91, 92, 93, 94, 95, 97, 98, 103, or 197; or

(iii) an amino acid sequence with 95-99% identity to any of SEQ ID NOs: 99, 96, 100, 101, 102, 91, 92, 93, 94, 95, 97, 98, 103, or 197.

23. The isolated nucleic acid molecule of any of the preceding claims, comprising the nucleotide sequence of any of SEQ ID NOs: 112, 109, 113, 114, 115, 104, 105, 106, 107, 108, 110, 111, 116, or 198, or a nucleotide sequence with 95-99% identity to any of SEQ ID NOs: 112, 109, 113, 114, 115, 104, 105, 106, 107, 108, 110, 111, 116,or 198.

24. An isolated polypeptide molecule encoded by the nucleic acid molecule of any one of claims 1-23.

25. An isolated chimeric antigen receptor (CAR) polypeptide, wherein the CAR comprises an antibody or antibody fragment which includes a human anti-CLL-1 binding domain, a transmembrane domain, and an intracellular signaling domain comprising a costimulatory domain and/or a primary signaling domain, and wherein said anti-CLL-1 binding domain comprises a heavy chain complementary determining region 1 (HC CDR1), a heavy chain complementary determining region 2 (HC CDR2), and a heavy chain complementary determining region 3 (HC CDR3) of any CLL-1 heavy chain binding domain amino acid sequences listed in Table 2.

26. The isolated CAR polypeptide of claim 25, wherein said anti-CLL-1 binding domain further comprises a light chain complementary determining region 1 (LC CDR1), a light chain complementary determining region 2 (LC CDR2), and a light chain complementary determining region 3 (LC CDR3) of any anti-CLL-1 light chain binding domain amino acid sequences listed in Table 2.

27. The isolated nucleic acid molecule of claim 26, wherein said LC CDR1, LC CDR2, and LC CDR3 are the LC CDR sequences listed in Table 6, 8, or 4.

28. The isolated nucleic acid molecules of any of claims 25-27, wherein said HC CDR1, HC CDR2, and HC CDR3 are the HC CDR sequences listed in Table 5, 7, or 3.

29. The isolated CAR polypeptide of any of claims 25-28, comprising:

(i) the amino acid sequence of any light chain variable region listed in Table 2;

(ii) an amino acid sequence having at least one, two or three modifications but not more than 30, 20 or 10 modifications of the amino acid sequence of any of the light chain variable region provided in Table 2; or

(iii) an amino acid sequence with 95-99% identity to the amino acid sequence of any of the light chain variable region provided in Table 2.

30. The isolated CAR polypeptide of any of claims 25-29, comprising:

(i) the amino acid sequence of any heavy chain variable region listed in Table 2;

(ii) an amino acid sequence having at least one, two or three modifications but not more than 30, 20 or 10 modifications of the amino acid sequence of any of the heavy chain variable region provided in Table 2: or

(iii) an amino acid sequence with 95-99% identity to the amino acid sequence of any of the heavy chain variable region provided in Table 2.

31. The isolated CAR polypeptide of any of claims 25-30, comprising the amino acid sequence of any light chain variable region listed in Table 2, and the amino acid sequence of any heavy chain variable region listed Table 2.

32. The isolated CAR polypeptide of any of claims 25-31, comprising:

(i) the amino acid sequence selected from a group consisting of SEQ ID NO: 47, 44, 48, 49, 50, 39, 40, 41, 42, 43, 45, 46, 51, 73, 70, 74, 75, 76, 65, 66, 67, 68, 69, 71, 72, 77, 195, 86, 83, 87, 88, 89, 78, 79, 80, 81, 82, 84, 85, 90, or 196;

(ii) an amino acid sequence having at least one, two or three modifications but not more than 30, 20 or 10 modifications to any of SEQ ID NO: 47, 44, 48, 49, 50, 39, 40, 41, 42, 43, 45, 46, 51, 73, 70, 74, 75, 76, 65, 66, 67, 68, 69, 71, 72, 77, 195, 86, 83, 87, 88, 89, 78, 79, 80, 81, 82, 84, 85, 90, or 196; or

(iii) an amino acid sequence with 95-99% identity to any of SEQ ID NO: 47, 44, 48, 49, 50, 39, 40, 41, 42, 43, 45, 46, 51, 73, 70, 74, 75, 76, 65, 66, 67, 68, 69, 71, 72, 77, 195, 86, 83, 87, 88, 89, 78, 79, 80, 81, 82, 84, 85, 90, or 196.

33. The isolated CAR polypeptide of any of claims 25-32, wherein the transmembrane domain comprises a transmembrane domain from 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, CD134, CD137 and CD154.

34. The isolated CAR polypeptide of any of claims 25-33, wherein:

(i) the transmembrane domain comprises the amino acid sequence of SEQ ID NO: 6,

(ii) an amino acid sequence comprises 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:6, or

(iii) a sequence with 95-99% identity to the amino acid sequence of SEQ ID NO:6.

35. The isolated CAR polypeptide of any of claims 25-34, wherein the CLL-1 binding domain is connected to the transmembrane domain by a hinge region.

36. The isolated CAR polypeptide of claim 35, wherein the hinge region comprises SEQ ID NO:2, or a sequence with 95-99% identity thereof.

37. The isolated CAR polypeptide of any of claims 25-36, wherein the costimulatory domain is a functional signaling domain obtained from a protein selected from the group consisting of a MHC class I molecule, TNF receptor proteins, Immunoglobulin-like proteins, cytokine receptors, integrins, signaling lymphocytic activation molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, OX40, CD2, CD7, CD27, CD28, CD30, CD40, CDS, ICAM-1, LFA-1 (CD11a/CD18), 4-1BB (CD137), B7-H3, CDS, ICAM-1, ICOS (CD278), GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL2R beta, IL2R gamma, IL7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, NKG2C, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, and a ligand that specifically binds with CD83.

38. The isolated CAR polypeptide of any of claims 25-37, wherein the costimulatory domain comprises the amino acid sequence of SEQ ID NO:7, or 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:7, or a sequence with 95-99% identity to the amino acid sequence of SEQ ID NO:7.

39. The isolated CAR polypeptide of any of claims 25-37, wherein the intracellular signaling domain comprises a functional signaling domain of 4-1BB and/or a functional signaling domain of CD3 zeta.

40. The isolated CAR polypeptide of any of claims 25-39, wherein the intracellular signaling domain comprises the amino acid sequence of SEQ ID NO: 7 and/or the sequence of SEQ ID NO:9 or SEQ ID NO:10; or 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:7 and/or the amino acid sequence of SEQ ID NO:9 or SEQ ID NO:10; or a sequence with 95-99% identity to the amino acid sequence of SEQ ID NO:7 and/or the amino acid sequence of SEQ ID NO:9 or SEQ ID NO:10.

41. The isolated CAR polypeptide of any of claims 25-40, wherein the intracellular signaling domain comprises the sequence of SEQ ID NO:7 and the sequence of SEQ ID NO:9 or SEQ ID NO:10, wherein the sequences comprising the intracellular signaling domain are expressed in the same frame and as a single polypeptide chain.

42. The isolated CAR polypeptide of any of claims 25-41, further comprising a leader sequence which comprises the amino acid sequence of SEQ ID NO:1.

43. The isolated CAR polypeptide of any of claims 25-42, comprising:

(i) the amino acid sequence of any of SEQ ID NOs: 99, 96, 100, 101, 102, 91, 92, 93, 94, 95, 97, 98, 103, or 197;

(ii) an amino acid sequence having at least one, two or three modifications but not more than 30, 20 or 10 modifications to any of SEQ ID NOs: 99, 96, 100, 101, 102, 91, 92, 93, 94, 95, 97, 98, 103, or 197; or

(iii) an amino acid sequence with 95-99% identity to any of SEQ ID NOs: 99, 96, 100, 101, 102, 91, 92, 93, 94, 95, 97, 98, 103, or 197.

44. A vector comprising a nucleic acid molecule encoding a CAR or an anti- CLL-1 binding domain of any of the preceding claims, wherein the vector is selected from the group consisting of a DNA vector, an RNA vector, a plasmid, a lentivirus vector, adenoviral vector, or a retrovirus vector.

45. The vector of claim 44, further comprising an EF-1 promoter comprising the sequence of SEQ ID NO: 11.

46. A cell, e.g., an immune effector cell, comprising nucleic acid of any of claims 1-23, the CAR polypeptide of any of claims 24-43, or the vector of claim 44 or 45.

47. A method of making a cell, e.g., an immune effector cell, comprising transducing an immune effector cell with a vector of either of claim 44 or 45.

48. A method of generating a population of RNA-engineered cells, comprising introducing an in vitro transcribed RNA or synthetic RNA into a cell, where the RNA comprises a nucleic acid encoding a CAR polypeptide of any of the preceding claims.

49. A cell, e.g., a population of immune effector cells, comprising the CAR nucleic acid of any of claims 1-23, or the CAR polypeptide of any of claims 24-43 for use in a method of providing an anti-tumor immunity in a mammal.

50. The cell for use according to claim 49, wherein the cell is an autologous T cell or an allogeneic T cell.

51. A cell, e.g., a population of immune effector cells, comprising the CAR nucleic acid of any of claims 1-23, or the CAR polypeptide of any of claims 24-43 for use in a method of treating a mammal having a disease associated with expression of CLL-1.

52. The cell for use according to claim 51, wherein the disease associated with CLL-1 expression is:

(i) a cancer or malignancy, or a precancerous condition chosen from one or more of a myelodysplasia, a myelodysplastic syndrome or a preleukemia, or

(ii) a non-cancer related indication associated with expression of CLL-1.

53. The cell for use according to claim 51 or 52, wherein the disease is a hematologic cancer.

54. The cell for use according to any of claims 51-53, wherein the disease is an acute leukemia chosen from one or more of acute myeloid leukemia (AML); acute lymphoblastic B-cell leukemia (B-cell acute lymphoid leukemia, BALL), acute lymphoblastic T-cell leukemia (T-cell acute lymphoid leukemia (TALL), B-cell prolymphocytic leukemia, chronic lymphocytic leukemia, chronic myeloid leukemia (CML), myelodysplastic syndrome, plasma cell myeloma, or a combination thereof.

55. The cell for use according to any of claims 51-54, wherein the cell, e.g., the population of immune effector cells, are to be administered in combination with one or more of:

(i) an agent that increases the efficacy of the cell comprising the CAR nucleic acid or CAR polypeptide;

(ii) an agent that ameliorates one or more side effects associated with administration of the cell comprising the CAR nucleic acid or CAR polypeptide; or

(iii) an agent that treats the disease associated with the expression of CLL-1.

56. The isolated nucleic acid molecule of any of claims 1-23, the isolated CAR polypeptide molecule of any of claims 24-43, , the vector of either of claim 44 or 45, or the cell of claim 46 for use as a medicament.

57. The isolated nucleic acid molecule of any of claims 1-23, the isolated CAR polypeptide molecule of any of claims 24-43, , the vector of either of claim 44 or 45, or the cell of claim 46 for use in the treatment of a disease associated with expression of CLL-1.

58. A cell, e.g., a population of immune effector cells, of claim 46, 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.

59. The cell of claim 58, wherein the inhibitory molecule comprise first polypeptide that comprises at least a portion of PD1 and a second polypeptide comprising a costimulatory domain and primary signaling domain.

60. The cell for use according to claim 55, wherein the agent is an mTOR inhibitor and the subject is to be administered a low, immune enhancing, dose of an mTOR inhibitor, e.g., RAD001 or rapamycin.

61. The cell for use according to claim 60, wherein the mTOR inhibitor is to be administered for an amount of time sufficient to decrease the proportion of PD-1 positive T cells, increase the proportion of PD-1 negative T cells, or increase the ratio of PD-1 negative T cells/ PD-1 positive T cells, in the peripheral blood of the subject, or in a preparation of T cells isolated from the subject.

62. A cell comprising the CAR nucleic acid molecule of any of claims 1-23 or the CAR polypeptide of any of claims 24-43 for use in a method of conditioning a subject prior to cell transplantation.

63. The cell for use according to claim 62, wherein the cell transplantation is a stem cell transplantation, e.g., a hematopoietic stem cell transplantation, or a bone marrow transplantation.

64. The cell for use according to either of claim 62 or 63, wherein conditioning a subject prior to cell transplantation comprises reducing the number of CLL-1 -expressing cells in a subject, e.g., CLL-1 -expressing normal cells or CLL-1 -expressing cancer cells.

65. The cell for use according to any of claims 51-54, wherein a chemotherapeutic agent is to be administered prior to administration of the cell, e.g., the population of immune effector cells; and optionally, wherein the chemotherapeutic agent increases CLL-1 expression on the cancer cell or wherein the chemotherapeutic agent is cytarabine.