for said hematologic malignancy that used a **CD123 x CD3** bispecific molecule; The disclosure further provides the example of such methods wherein such method further comprises administering a treatment dosage of the **CD123 x CD3** bispecific molecule to the patient if the patient is determined to be a suitable responder to such treatment, and to such methods wherein the administration of the **CD123 x CD3** bispecific molecule stimulates the killing of cells of the hematologic malignancy in the patient.

[0027] The disclosure further provides a method of treating a hematologic malignancy, wherein the method comprises:

(a) employing the method of any one of the above examples to determine whether a patient would be a suitable responder to the use of a **CD123 x CD3** bispecific molecule to treat the hematologic malignancy;

(b) administering a treatment dosage of the **CD123 x CD3** bispecific molecule to the patient if the patient is determined to be a suitable responder to such treatment;

wherein the administration of the **CD123 x CD3** bispecific molecule stimulates the killing of cells of the hematologic malignancy in the patient.

[0027a] In one example, the present disclosure refers to use of a **CD123 x CD3** bispecific molecule in the manufacture of a medicament for treating a hematologic malignancy, wherein a treatment dosage of said **CD123 x CD3** bispecific molecule is to be administered to a patient who has been determined to be a suitable responder to such treatment, wherein said determination of suitability comprises:

(a) evaluating the expression of one or more target genes in a cellular sample from said patient prior to the administration of said **CD123 x CD3** bispecific molecule, relative to the expression of one or more target and/or reference genes; and

(b) identifying the patient as a suitable responder for treatment with a **CD123 x CD3** bispecific molecule if the expression of said one or more target genes is found to be increased relative to said expression of said one or more target and/or reference genes, wherein said one or more target genes are selected from the group consisting of: SERPHINH1, NOTCH2, FCGR3A/B, FPR1, FBP1, PDGFA, CRABP2, THBS1, ICOS and CD8B;

wherein said administration of said **CD123 x CD3** bispecific molecule stimulates the killing of cells of said hematologic malignancy in said patient.

In one aspect, the present disclosure refers to use of a **CD123 x CD3** bispecific molecule in the manufacture of a medicament for treating a hematologic malignancy, wherein a treatment dosage of said **CD123 x CD3** bispecific molecule is to be administered to a patient who has been determined to be a suitable responder to such treatment, wherein said determination of suitability comprises:

(a) evaluating the expression of a gene expression signature in a cellular sample from said patient prior to the administration of said **CD123 x CD3** bispecific molecule, relative to the expression of said gene expression signature of:

(i) an individual who is suffering from said hematologic malignancy, or of a population of such individuals; or

(ii) an individual who did not successfully respond to the use of a **CD123 x CD3** bispecific molecule to treat said hematologic malignancy, or of a population of such individuals; or

(iii) an individual who successfully responded to the use of a **CD123 x CD3** bispecific molecule to treat said hematologic malignancy, or of a population of such individuals; and

(b) identifying the patient as a suitable responder for treatment with a **CD123 x CD3** bispecific molecule if the expression of said gene expression signature is found to be increased relative to said expression of said gene expression signature of an individual or population of such individuals listed in (i)-(iii) above, wherein said gene expression signature consists of the expression of from six to ten genes selected from: SERPINH1, NOTCH2, FCGR3A/B, FPR1, FBP1, PDGFA, CRABP2, THBS1, ICOS and CD8B;

wherein said administration of said **CD123 x CD3** bispecific molecule stimulates the killing of cells of said hematologic malignancy in said patient.

[0028] The disclosure further provides the example of such methods that additionally comprises evaluating the expression of such one or more target genes in a cellular sample obtained from the patient one or more times after the initiation of the treatment.

[0029] The disclosure further provides the example of such methods wherein the cellular sample is a bone marrow or a blood sample. Particularly, the example of such methods wherein the cellular sample is a bone marrow sample.

[0030] The disclosure further provides the example of such methods that further comprises detecting the expression level of one or more target genes in a sample of the patient's bone marrow. The disclosure further provides the example of such methods that further comprises detecting the expression level of one or more reference genes.

WHAT IS CLAIMED IS:

Claim 1. Use of a **CD123 x CD3** bispecific molecule in the manufacture of a medicament for treating a hematologic malignancy, wherein a treatment dosage of said **CD123 x CD3** bispecific molecule is to be administered to a patient who has been determined to be a suitable responder to such treatment, wherein said determination of suitability comprises:

(a) evaluating the expression of a gene expression signature in a cellular sample from said patient prior to the administration of said **CD123 x CD3** bispecific molecule, relative to the expression of said gene expression signature of:

(i) an individual who is suffering from said hematologic malignancy, or of a population of such individuals; or

(ii) an individual who did not successfully respond to the use of a **CD123 x CD3** bispecific molecule to treat said hematologic malignancy, or of a population of such individuals; or

(iii) an individual who successfully responded to the use of a **CD123 x CD3** bispecific molecule to treat said hematologic malignancy, or of a population of such individuals; and

(b) identifying the patient as a suitable responder for treatment with a **CD123 x CD3** bispecific molecule if the expression of said gene expression signature is found to be increased relative to said expression of said gene expression signature of an individual or population of such individuals listed in (i)-(iii) above, wherein said gene expression signature consists of the expression of from six to ten genes selected from: SERPINH1, NOTCH2, FCGR3A/B, FPR1, FBP1, PDGFA, CRABP2, THBS1, ICOS and CD8B;

wherein said administration of said **CD123 x CD3** bispecific molecule stimulates the killing of cells of said hematologic malignancy in said patient.

Claim 2. The use of claim 1, wherein said hematologic malignancy of said patient is selected from the group consisting of: acute myeloid leukemia (AML), chronic myelogenous leukemia (CML), blastic crisis of CML, Abelson oncogene-associated with CML (Bcr-ABL translocation), myelodysplastic syndrome (MDS), acute B lymphoblastic leukemia (B-ALL), acute T lymphoblastic leukemia (T-ALL), chronic lymphocytic leukemia (CLL), Richter's syndrome, Richter's transformation of CLL, hairy cell leukemia (HCL), blastic plasmacytoid dendritic cell neoplasm (BPDCN), non-Hodgkin's lymphoma (NHL), including mantle cell lymphoma (MCL) and small lymphocytic lymphoma (SLL), Hodgkin's lymphoma, systemic mastocytosis, and Burkitt's lymphoma.

Claim 3. The use of claim 2, wherein said hematologic malignancy of said patient is AML.

Claim 4. The use of any one of claims 1-3, wherein said hematologic malignancy of said patient is refractory to chemotherapy.

Claim 5. The use of any one of claims 1-4, wherein said determination of suitability evaluates:

(i) the expression of said gene expression signature of said patient; and

(ii) the expression of one or more reference genes of said patient whose expression is not characteristically associated with said hematologic malignancy.

Claim 6. The use of claim 5, wherein said determination of suitability comprises determining whether said patient would be a suitable responder to such treatment by evaluating the expression of said gene expression signature

of said patient relative to the baseline expression of said one or more reference genes of said patient.

Claim 7. The use of any one of claims 1-6, wherein the relative expression level of said gene expression signature in said population is established by averaging the gene expression level in cellular samples obtained from said population of individuals.

Claim 8. The use of any one of claims 1-7, wherein said gene expression signature exhibits an expression level :

(a) that is greater than the first quartile of the expression levels of said gene expression signature in a population of individuals who are suffering from said hematologic malignancy; or

(b) that is greater than the first quartile of the expression levels of said gene expression signature in a population of individuals who did not successfully respond to a treatment for said hematologic malignancy that used a **CD123 x CD3** bispecific molecule; or

(c) that is within at least the first quartile of the expression levels of said gene expression signature in a population of individuals who successfully responded to a treatment for said hematologic malignancy that used a **CD123 x CD3** bispecific molecule.

Claim 9. The use of any one of claims 1-8, wherein said cellular sample is a bone marrow sample.

Claim 10. The use of any one of claims 1-9, wherein said determination of whether said patient would be a suitable responder to the use of a **CD123 x CD3** bispecific molecule to treat a hematologic malignancy is performed by:

(a) determining the gene expression levels for each gene in said gene expression signature in one or more cellular sample(s) using a gene expression platform; and

(b) comparing said gene expression signature levels to the expression levels of one or more reference genes.

Claim 11. The use of any one of claims 1-10, wherein said determination of whether a patient would be a suitable responder to the use of a **CD123 x CD3** bispecific molecule to treat a hematologic malignancy is performed by:

(a) measuring raw RNA levels for each gene in said gene expression signature in one or more cellular sample(s) using a gene expression platform, wherein the gene expression platform comprises a reference gene set of housekeeping genes, and

(b) assigning a relative expression value, for each of the measured raw RNA levels for each gene in said gene expression signature using the measured RNA levels of the internal reference genes.

Claim 12. The use of any one of claims 5-11, wherein said one or more reference genes comprise one or more of: ABCF1, G6PD, NRDE2, OAZ1, POLR2A, SDHA, STK11IP, TBC1D10B, TBP, and UBB.

Claim 13. The use of any one of claims 1-12, further comprising determining a gene signature score for said gene expression signature, wherein said gene signature score is determined by a process comprising:

(a) measuring raw RNA levels for each gene in said gene expression signature in one or more cellular sample(s) using a gene expression platform comprising a reference gene set of housekeeping genes;

(b) normalizing each of the measured raw RNA levels to the geometric mean of said housekeeping genes, and optionally further normalizing each RNA value to a standard;

(c) log transforming each normalized RNA value;

(d) summing the log transformed RNA values for each gene in the signature; and

(e) dividing the sum of the normalized log transformed RNA values by the number of genes in the signature, to generate a gene signature score.

Claim 14. The use of claim 13, wherein a patient gene signature score that:

(a) is greater than the first quartile of scores for said gene expression signature calculated from the expression levels of each gene in said gene expression signature in a population of individuals who are suffering from said hematologic malignancy; or

(b) is greater than the first quartile of scores for said gene expression signature calculated from the expression levels of each gene in said gene expression signature in a population of individuals who did not successfully respond to a treatment for said hematologic malignancy that used a **CD123 x CD3** bispecific molecule; or

(c) is within at least the first quartile of the scores for said gene expression signature calculated from the expression levels of each gene in said gene expression signature in a population of individuals who successfully responded to a treatment for said hematologic malignancy that used a **CD123 x CD3** bispecific molecule,

is indicative of a more favorable patient response to treatment with said **CD123 x CD3** bispecific molecule.

Claim 15. The use of any one of claims 1-14, wherein said **CD123 x CD3** bispecific molecule is a bispecific antibody or bispecific molecule comprising an scFv.

Claim 16. The use of claim 15, wherein said **CD123 x CD3** bispecific molecule is JNJ-63709178, XmAb14045 or APVO436.

Claim 17. The use of any one of claims 1-14, wherein said **CD123 x CD3** bispecific molecule is a covalently bonded bispecific diabody that comprises two, three, or four polypeptide chains.

Claim 18. The use of claim 17, wherein said covalently bonded bispecific diabody comprises a first polypeptide chain that comprises the amino acid sequence of **SEQ ID NO:21** covalently bonded via a disulfide bond to

a second polypeptide chain that comprises the amino acid sequence of **SEQ ID NO:23.**

Claim 19. The use of any one of claims 1-18, wherein said hematologic malignancy of said patient is refractory to chemotherapy.

Claim 20. The use of any one of claims 1-19, wherein said treatment dosage of said **CD123 x CD3** bispecific molecule includes at least one dose selected from the group consisting of about 30, about 60, about 100, about 200, about 300, about 400 and about 500ng/kg patient weight/day.

Claim 21. The use of any one of claims 1-20, wherein said treatment dosage is to be administered by continuous infusion.