CLAIMS

1. Use of

i) a multispecific protein comprising a CD123 binding domain and a CD3 binding domain; and

ii) a second anti-cancer agent

in the manufacture of a medicament for treating a cancer in a subject in need thereof,

wherein the second anti-cancer agent is venetoclax,

wherein the cancer is selected from the group consisting of acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), hairy cell leukemia (HCL), blastic plasmacytoid dendritic cell neoplasm, B-cell acute lymphoblastic leukemia (ALL), or chronic myeloid leukemia.

2. The use of claim 1, wherein a third anti-cancer agent is to be administered to the subject.

3. The use of claim 1 or 2, wherein the third anti-cancer agent is a chemotherapeutic drug,

and optionally wherein the chemotherapeutic drug is azacitidine, decitabine, daunorubicin, cytarabine, idarubicin, mitoxantrone, or etoposide.

4. The use of claim 1, wherein the venetoclax is to be administered at a dose of from about 100 to about 400 mg per day.

5. The use of any one of claims 1-4, wherein the multispecific protein comprises: a dimer of two identical polypeptides, wherein each polypeptide comprises, in order from amino-terminus to carboxyl-terminus, or in order from carboxyl-terminus to amino-terminus:

(i) a CD123 binding domain,

(ii) a hinge region,

(iii) an immunoglobulin constant region, and

(iv) a CD3 binding domain.

6. The use of claim 5, wherein the polypeptide comprises, from N-terminus to C-terminus, the CD123 binding domain, the hinge region, the immunoglobulin constant region, and the CD3 binding domain.

7. The use of claim 6, wherein at least one of the CD123 and the CD3 binding domains comprises:

(i) an immunoglobulin heavy chain variable region (VH) comprising HCDR1, HCDR2, and HCDR3; and

(ii) an immunoglobulin light chain variable region (VL) comprising LCDR1, LCDR2, and LCDR3.

8. The use of claim 7,

wherein the CD123 binding domain is a scFv comprising:

a HCDR1 that comprises SEQ ID NO: 10, a HCDR2 that comprises SEQ ID NO: 11, and a HDCR3 that comprises SEQ ID NO: 12; and

a LCDR1 that comprises SEQ ID NO: 13, a LCDR2 that comprises SEQ ID NO: 14, and a LCDR3 that comprises SEQ ID NO: 15;

or

wherein the CD123 binding domain is a scFv comprising:

a VH comprising a sequence at least 95%, or 100% identical to SEQ ID NO: 136, and

a VL comprising a sequence at least 95%, or 100% identical to SEQ ID NO: 134;

or

wherein the CD123 binding domain is a scFv, and wherein the scFv comprises a sequence at least 95%, or 100% identical to SEQ ID NO: 18.

9. The use of claim 7 or 8,

wherein the CD3 binding domain is a scFv comprising:

a HCDR1 that comprises SEQ ID NO: 19, a HCDR2 that comprises SEQ ID NO: 20, and a HDCR3 that comprises SEQ ID NO: 21; and

a LCDR1 that comprises SEQ ID NO: 22, a LCDR2 that comprises SEQ ID NO: 23, and a LCDR3 that comprises SEQ ID NO: 24;

or

wherein the CD3 binding domain is a scFv that comprises:

a VH comprising a sequence at least 95%, or 100% identical to SEQ ID NO: 383 or 387, and

a VL comprising a sequence at least 95%, or 100% identical to SEQ ID NO: 384;

or

wherein the CD3 binding domain is a scFv that comprises a sequence at least 95%, or 100% identical to SEQ ID NO: 27.

10. The use of claim 7, wherein each polypeptide comprises a sequence at least 95%, or 100% identical to SEQ ID NO: 31.

11. The use of any one of claims 1-10, wherein the multispecific protein is to be administered to the subject by IV infusion.

12. The use of any one of claims 1-11, wherein the second anti-cancer agent is to be administered to the subject orally.

13. The use of any one of claims 1-12, wherein the multispecific protein is to be administered the subject by IV infusion at a dose of 0.3, 1, 3, 6, 9, 12, 18, 20, 24, 30, 36, 48, 50, 60, 75, or 100 μg.

14. The use of any one of claims 1-13, wherein the multispecific protein is to be administered once per week.

15. The use of claim 14, wherein the multispecific protein is to be administered to the subject by IV infusion during a first 28-day cycle; wherein 6 μg of the multispecific protein is to be administered on day 8; 12 μg of the multispecific protein is to be administered on day 15; and 18 μg of the multispecific protein is to be administered on day 22 of the first 28-day cycle,

and optionally wherein the multispecific protein is to be administered to the subject by IV infusion during at least one additional 28-day cycle following the first 28-day cycle, wherein 18 μg of the multispecific protein is to be administered on days 1, 8, 15, and 22 of the at least one additional 28-day cycle.

16. The use of claim 14, wherein the multispecific protein is to be administered to the subject by IV infusion during a first 28-day cycle; wherein 6 μg of the multispecific protein is to be administered on day 15; and 12 μg of the multispecific protein is to be administered on day 22 of the first 28-day cycle,

optionally wherein the multispecific protein is to be administered to the subject by IV infusion during at least one additional 28-day cycle following the first 28-day cycle, wherein 18

μg of the multispecific protein is to be administered on days 1, 8, 15, and 22 of the at least one additional 28-day cycle,

optionally wherein venetoclax is to be administered orally on days 1-21 of the first 28-day cycle, and days 1-21 of at least one additional 28-day cycle,

optionally wherein the dose of venetoclax is from about 100 to about 400 mg/day,