CLAIMS

~~1. A method of treating a patient having relapsed and/or refractory multiple myeloma comprising administering to the patient~~Use of an antibody that specifically binds CD38~~, wherein said antibody is administered to the patient in a safe therapeutic dose~~ in the manufacture of ~~20 mg/kg or below.~~

1. ~~2. A pharmaceutical composition comprising an antibody that specifically binds CD38 for use as~~ a medicament ~~in~~for the treatment of relapsed and/or refractory multiple myeloma in a human subject, wherein~~-~~:

said antibody comprises at least one heavy chain and at least one light chain;

said heavy chain comprises three sequential complementarity-determining regions (CDRs) comprising the amino acid sequences of SEQ ID NOs: 13, 37, and 15;

said light chain comprises three sequential complementarity-determining regions (CDRs) comprising the amino acid sequences of SEQ ID NOs: 16, 17, and 18; and

said antibody is formulated for administration to ~~be administered to a~~the human subject in a safe therapeutic dose of ~~about~~10 mg/kg or 20 mg/kg ~~or less~~once every two weeks.

~~3.~~

2. The ~~method or pharmaceutical composition according to claims 1 or 2~~use of claim 1, wherein the antibody is capable of killing a $CD38^{+}$~~-~~ cell in the human subject by induction of apoptosis, antibody-dependent cell-mediated cytotoxicity (ADCC), and complement-dependent cytotoxicity (CDC).

~~4.~~

3. The ~~method or pharmaceutical composition according any one~~use of ~~claims~~claim 1 ~~to 3~~or 2, wherein the ~~patient~~human subject has at least one condition selected from the group consisting of

a) measurable serum M-protein level greater than about 0.5 g/dL,

b) urine M-protein level greater than about 200 mg (24-hr urine),

c) elevated level of serum free light chains (FLC) greater than about 10 mg/dL with abnormal FLC ratio,

and combination thereof.

~~5.~~

The ~~method or pharmaceutical composition according to~~ use of any one of claims 1~~ to 4, wherein said antibody comprises at least one heavy chain and at least one light chain, wherein said heavy chain comprises three sequential complementarity-determining regions (CDRs) having amino acid sequences represented by SEQ ID NOS: 13, 37, and 15, and wherein said~~

~~light chain comprises three sequential complementarity determining regions (CDRs) having amino acid sequences represented by SEQ ID NOS: 16, 17, and 18.~~

4. ~~6. The method or pharmaceutical composition according to any one of claims 1 to 5~~3, wherein said antibody comprises at least one heavy chain comprising an amino acid sequence ~~represented by~~of SEQ ID NO: 50 and at least one light chain comprising an amino acid sequence ~~represented by~~of SEQ ID NO: 52.

~~7.~~

5. The ~~method or pharmaceutical composition according to~~ use of any one of claims 1~~ to 6~~4, wherein the safe therapeutic dose of said antibody is ~~from about 1 mg/kg to about 20 mg/kg~~to be administered intravenously.

~~8. The method or pharmaceutical composition according to any one of claims 1 to 6, wherein the safe therapeutic dose is about 5 mg/kg, or about 10 mg/kg, or about 20 mg/kg.~~

~~9. The method or pharmaceutical composition according to any one of claims 1 to 8~~

The use of claims 5, wherein the safe therapeutic dose of said antibody is ~~administered intravenously.~~

~~10. The method or pharmaceutical composition according to any one of claims 1 to 9, wherein the safe therapeutic dose of said antibody is administered once a week or once every two weeks.~~

~~11. The method or pharmaceutical composition according to any one of claims 1 to 10, wherein the safe therapeutic dose is about 10 mg/kg or about 20 mg/kg administered once every two weeks.~~

~~12. The method or pharmaceutical composition according to any one of claims 1 to 10, wherein the safe therapeutic dose is about 10 mg/kg or about 20 mg/kg administered once every week.~~

6. ~~13. The method or pharmaceutical composition according to any one of claims 1 to 12, wherein the safe therapeutic dose of said antibody is~~to be administered at an initial rate of infusion ranging from about 0.042 mg/hr to about 250 mg/hr.

~~14.~~

7. The ~~method or pharmaceutical composition according to~~ use of any one of claims 1~~ to 13~~6, wherein the antibody is to be administered in combination with dexamethasone.

~~15.~~

The ~~method or pharmaceutical composition according to~~ use of any one of claims 1~~ to 14~~-7, wherein said antibody does not produce autoantibodies against said antibody ~~when administered to a human subject at a dose of about 20 mg/kg or less.~~

8. ~~16. The method or pharmaceutical composition according to any one of claims 1 to 10, wherein said antibody is capable of exhibiting detectable CD38 receptor occupancy~~ in a human subject ~~when administered to said human subject at a dose level of about 1 mg/kg every two weeks~~.

~~17.~~

9. The ~~method or pharmaceutical composition according to~~ use of any one of claims 1~~ to 10~~-8, wherein said antibody is capable of exhibiting at least about 84.1% CD38 receptor occupancy in a human subject ~~when administered to said human subject at a dose level of about 10 mg/kg or about 20 mg/kg every two weeks~~.

~~18.~~

10. The ~~method or pharmaceutical composition according to~~ use of any one of claims 1~~ to 10~~-9, wherein said antibody is capable of exhibiting at least about 97.7% CD38 receptor occupancy in a human subject ~~when administered to said human subject at a dose level of about 10 mg/kg or about 20 mg/kg every two weeks~~.

~~19.~~

11. The ~~method or pharmaceutical composition according to~~ use of any one of claims 1~~ to -~~10, wherein said antibody is capable of inhibiting tumor growth in a human subject ~~when administered to said human subject at a dose level ranging from about 5 mg/kg to about 20 mg/kg every two weeks~~.

~~20.~~

12. The ~~method or pharmaceutical composition according to~~ use of any one of claims 1~~ to 10~~-11, wherein ~~said antibody is capable~~the human subject has received prior anti-cancer therapy.

13. The use of ~~inhibiting tumor growth in a~~claim 12, wherein:

the human subject ~~when administered to said~~has received at least two prior anti-cancer therapies, or

the human subject ~~at a dose level ranging from about 5 mg/kg to about 20 mg/kg every week.~~has received at least three prior anti-cancer therapies, or

~~21. The method or pharmaceutical composition according to any one of claims 1 to 10, wherein said antibody is capable of inhibiting tumor growth in a human subject when administered to said human subject at a dose level ranging from about 10 mg/kg to about 20 mg/kg every two weeks.~~

~~22. The method or pharmaceutical composition according to any one of claims 1 to 10, wherein said antibody is capable of inhibiting tumor growth in a human subject when administered to said human subject at a dose level ranging from about 10 mg/kg to about 20 mg/kg every week.~~

~~23. A unit dosage form comprising the pharmaceutical composition of any one of claims 1 to 22.~~

~~24. An article of manufacture comprising the pharmaceutical composition of any one of claims 1 to 22 and a container.~~

the human subject has received 2 to 14 prior anti-cancer therapies.

14. The use of claim 12 or 13, wherein:

the human subject has been treated with bortezomib as prior anti-cancer therapy;

the human subject has been treated with lenalidomide as prior anti-cancer therapy; or

the human subject has been treated with bortezomib and lenalidomide as prior anti-cancer therapy.