

CLAIMS

1. An anti-CD38 antibody comprising (a) a heavy chain variable domain (V_H) that comprises: a CDR-H1 comprising the amino acid sequence DYWMQ (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence TIYPGDGDTGYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence GDYYGSNSLDY (SEQ ID NO: 3), and (b) a light chain variable domain (V_L) that comprises: a CDR-L1 comprising the amino acid sequence KASQDVSTVVA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence SASYRYI (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQHYSPPYT (SEQ ID NO: 6) for use in a method of treating multiple myeloma in an individual, the method comprising administering the anti-CD38 antibody, carfilzomib, and dexamethasone to the individual,

wherein the anti-CD38 antibody is administered at a dose of 10 mg/kg, the carfilzomib is administered at a dose of 20 mg/m² or 56 mg/m², and the dexamethasone is administered at a dose of 20 mg,

wherein the individual received at least one prior therapy for multiple myeloma, and wherein the treatment extends progression free survival (PFS) and/or overall survival (OS) of the individual.

2. An anti-CD38 antibody comprising (a) a heavy chain variable domain (V_H) that comprises: a CDR-H1 comprising the amino acid sequence DYWMQ (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence TIYPGDGDTGYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence GDYYGSNSLDY (SEQ ID NO: 3), and (b) a light chain variable domain (V_L) that comprises: a CDR-L1 comprising the amino acid sequence KASQDVSTVVA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence SASYRYI (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQHYSPPYT (SEQ ID NO: 6) for use in a method of treating multiple myeloma in an individual, the method comprising the method comprising administering the anti-CD38 antibody, carfilzomib, and dexamethasone to the individual,,

wherein the anti-CD38 antibody is administered at a dose of 10 mg/kg, the carfilzomib is administered at a dose of 20 mg/m² or 56 mg/m², and the dexamethasone is administered at a dose of 20 mg,

wherein the individual received at least one prior therapy for multiple myeloma, and

wherein the individual is Minimal Residual Disease negative at a threshold of 10⁻⁵ or less after treatment.

3. An anti-CD38 antibody comprising (a) a heavy chain variable domain (V_H) that comprises: a CDR-H1 comprising the amino acid sequence DYWMQ (SEQ ID NO: 1), a CDR-H2

comprising the amino acid sequence TIYPGDGDTGYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence GDYYGSNSLDY (SEQ ID NO: 3), and (b) a light chain variable domain (V_L) that comprises: a CDR-L1 comprising the amino acid sequence KASQDVSTVVA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence SASYRYI (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQHYSPPYT (SEQ ID NO: 6) for use in a method of treating multiple myeloma in an individual, the method comprising administering the anti-CD38 antibody, carfilzomib and dexamethasone to the individual,

wherein the anti-CD38 antibody is administered at a dose of 10 mg/kg, the carfilzomib is administered at a dose of 20 mg/m² or 56 mg/m², and the dexamethasone is administered at a dose of 20 mg,

wherein the individual received at least one prior therapy for multiple myeloma, and wherein the individual has renal impairment at the start of treatment.

4. The anti-CD38 antibody for use according to any one of claims 1-3, wherein the individual received 1-3 prior therapies for multiple myeloma, and wherein the treatment extends progression free survival (PFS) and/or overall survival (OS) of the individual.
5. The anti-CD38 antibody for use according to any one of claims 1-3, wherein the individual received 1-3 prior therapies for multiple myeloma.
6. The anti-CD38 antibody for use according to any one of claims 1-3, wherein the individual received more than three prior therapies for multiple myeloma.
7. The anti-CD38 antibody for use according to any one of claims 1-3, wherein the individual received prior therapy with a proteasome inhibitor.
8. The anti-CD38 antibody for use according to any one of claims 1-3, wherein the individual received prior therapy with an immunomodulatory agent.
9. The anti-CD38 antibody for use according to any one of claims 1-3, wherein the individual is classified as Stage I or Stage II according to the Revised International Staging System for multiple myeloma (R-ISS) at the start of treatment.
10. The anti-CD38 antibody for use according to any one of claims 1-3, wherein the individual is classified as Stage III according to R-ISS at the start of treatment.
11. The anti-CD38 antibody for use according to any one of claims 1-3, wherein the

individual is not classified according to R-ISS at the start of treatment.

12. The anti-CD38 antibody for use according to any one of claims 1-3, wherein the individual has one or more cytogenetic abnormalities selected from the group consisting of: del(17p), t(4;14), and t(14;16).

13. The anti-CD38 antibody for use according to any one of claims 1 or 2, wherein the individual has renal impairment at the start of treatment.

14. The anti-CD38 antibody for use according to any one of claims 1-3, wherein the individual is 65 to less than 75 years of age at the start of treatment.

15. The anti-CD38 antibody for use according to any one of claims 1-3, wherein the individual is 75 years of age or older at the start of treatment.

16. The anti-CD38 antibody for use according to any one of claims 1-3, wherein the anti-CD38 antibody comprises a heavy chain variable region (V_H) comprising an amino acid sequence of SEQ ID NO: 7 and a light chain variable region (V_L) comprising an amino acid sequence of SEQ ID NO: 7 or SEQ ID NO: 9.

17. The anti-CD38 antibody for use according to any one of claims 1-3, wherein the anti-CD38 antibody is isatuximab.

18. The anti-CD38 antibody for use according to any one of claims 1-3, wherein the anti-CD38 antibody, the carfilzomib, and the dexamethasone are administered in a first 28-day cycle, wherein, the anti-CD38 antibody is administered at the dose of 10 mg/kg on Days 1, 8, 15, and 22 of the first 28-day cycle, the carfilzomib is administered at the dose of 20 mg/m² on Days 1 and 2 and at a dose of 56 mg/m² on Days 8, 9, 15, and 16 of the first 28-day cycle, and the dexamethasone is administered at the dose 20 mg on Days 1, 2, 8, 9, 15, 16, 22, and 23 of the first 28-day cycle.

19. The anti-CD38 antibody for use according to claim 18, wherein the anti-CD38 antibody, the carfilzomib, and the dexamethasone are further administered in one or more 28-day cycles following the first 28-day cycle,

wherein the anti-CD38 antibody is administered at the dose of 10 mg/kg on Days 1 and 15 of the one or more 28-day cycles following the first 28-day cycle, the carfilzomib is administered at a dose of 56 mg/m² on each of Days 1, 2, 8, 9, 15, and 16 of the one or more one or more 28-day

cycles following the first 28-day cycle, and the dexamethasone is administered at the dose 20 mg on Days 1, 2, 8, 9, 15, 16, 22, and 23 of the one or more one or more 28-day cycles following the first 28-day cycle.

20. The anti-CD38 antibody for use according to any one of claims 1 or 3, wherein the individual is MRD negative at a threshold of 10^{-5} or less after treatment.

21. A method of treating a human individual having multiple myeloma, comprising administering to the individual an anti-CD38 antibody comprising (a) a heavy chain variable domain (V_H) that comprises: a CDR-H1 comprising the amino acid sequence DYWMQ (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence TIYPGDGDTGYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence GDYYGSNSLDY (SEQ ID NO: 3), and (b) a light chain variable domain (V_L) that comprises: a CDR-L1 comprising the amino acid sequence KASQDVSTVVA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence SASYRYI (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQHYSPPYT (SEQ ID NO: 6), carfilzomib, and dexamethasone,

wherein the anti-CD38 antibody is administered at a dose of 10 mg/kg, the carfilzomib is administered at a dose of 20 mg/m² or 56 mg/m², and the dexamethasone is administered at a dose of 20 mg,

wherein the individual received at least one prior therapy for multiple myeloma, and wherein the treatment extends progression free survival (PFS) of the individual.

22. The method of claim 21, wherein the treatment extends overall survival (OS) of the individual.

23. A method of treating a human individual having multiple myeloma, comprising administering to the individual an anti-CD38 antibody comprising (a) a heavy chain variable domain (V_H) that comprises: a CDR-H1 comprising the amino acid sequence DYWMQ (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence TIYPGDGDTGYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence GDYYGSNSLDY (SEQ ID NO: 3), and (b) a light chain variable domain (V_L) that comprises: a CDR-L1 comprising the amino acid sequence KASQDVSTVVA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence SASYRYI (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQHYSPPYT (SEQ ID NO: 6), carfilzomib, and dexamethasone,

wherein the anti-CD38 antibody is administered at a dose of 10 mg/kg, the carfilzomib is administered at a dose of 20 mg/m² or 56 mg/m², and the dexamethasone is administered at a dose of 20 mg,

wherein the individual received at least one prior therapy for multiple myeloma, and
wherein the treatment extends overall survival (OS) of the individual.

24. A method of treating a human individual having multiple myeloma, comprising administering to the individual an anti-CD38 antibody comprising (a) a heavy chain variable domain (V_H) that comprises: a CDR-H1 comprising the amino acid sequence DYWMQ (SEQ ID NO: 1), a CDR-H2 comprising the amino acid sequence TIYPGDGDTGYAQKFQG (SEQ ID NO: 2), and a CDR-H3 comprising the amino acid sequence GDYYGSNSLDY (SEQ ID NO: 3), and (b) a light chain variable domain (V_L) that comprises: a CDR-L1 comprising the amino acid sequence KASQDVSTVVA (SEQ ID NO: 4), a CDR-L2 comprising the amino acid sequence SASYRYI (SEQ ID NO: 5), and a CDR-L3 comprising the amino acid sequence QQHYSPPYT (SEQ ID NO: 6), carfilzomib, and dexamethasone,

wherein the anti-CD38 antibody is administered at a dose of 10 mg/kg, the carfilzomib is administered at a dose of 20 mg/m² or 56 mg/m², and the dexamethasone is administered at a dose of 20 mg,

wherein the individual received at least one prior therapy for multiple myeloma, and

wherein the individual is Minimal Residual Disease negative at a threshold of 10⁻⁵ or less after treatment.