SUMMARY

In one ~~aspect~~example, this application is based in part on the discovery of methods that result in, e.g., one or more of: a therapeutically desired steady-state concentration of an anti-BCMA antibody in the serum of a subject, a therapeutically desired reduction in the steady-state levels of free light chain in the serum of a subject, and a therapeutically desired saturation of BCMA in a subject.

In another ~~aspect~~example, this application is based upon evidence demonstrating the efficacy of combining certain BCMA therapeutic agents such as BCMA antibodies, including non-fucosylated antibodies, with various other therapeutics to treat cancers such as MM. Therapeutics found to successfully combine with such BCMA agents (e.g., non-fucosylated antibodies) include dexamethasone, an immunomodulatory agent (an IMiD) (e.g., pomalinamide), an CD38 antibody (e.g., daratumumab), and/or a gamma secretase inhibitor (GSI), including all the various combinations of these therapeutic agents.

In yet another ~~aspect~~example, the application is based in part on the identification of various BCMA antibody dosing regimens, including a standard and an intensive dosing regimen (defined more fully below) that have been shown to be therapeutically efficacious as monotherapy as well as in combination therapy, including combinations with dexamethasone, an IMiD (e.g., pomalinamide), an CD38 antibody (e.g., daratumumab), and/or a GSI. These results were unexpected given that a relatively high level of a BCMA antibody as described herein could be administered while still maintaining a manageable safety profile, including even when the BCMA antibody was administered as part of a combination therapy.

Accordingly, provided herein are methods of treating a subject having multiple myeloma (MM), the method comprising administering to the subject one or more doses of an antibody, or antigen binding fragment thereof, that specifically binds to a B cell maturation antigen (BCMA), and wherein the one or more doses are independently administered to the subject at about 100 mg of the antibody or antigen-binding fragment to about 2,000 mg of the antibody or antigen-binding fragment.

In one aspect, the present disclosure refers to use of an antibody, or antigen binding fragment thereof, that specifically binds to a B cell maturation antigen (BCMA), in the manufacture of a medicament for treating multiple myeloma (MM)in a subject in need, wherein one or more doses are to be independently administered to the subject at about 100 mg of the antibody or antigen-binding fragment to about 2,000 mg of the antibody or antigen-binding fragment.

In some ~~embodiment~~examples of any of the methods described herein, the antibody or antigen-binding fragment thereof is a non-fucosylated antibody or antigen-binding fragment.

In some ~~embodiment~~examples, a composition comprising the antibody or antigen-binding fragment thereof is administered to the subject. In some ~~embodiment~~examples, about or at least 95%,

97%, 98% or 99% of the antibody or antigen-binding fragment thereof in the composition are afucosylated.

In some ~~embodiment~~examples of any of the methods described herein, the antibody or antigen binding-fragment thereof, comprises: a heavy chain variable region comprising a CDR1 comprising SEQ ID NO: 1, a CDR2 comprising SEQ ID NO: 2, and a CDR3 comprising SEQ ID NO: 3, and a light chain variable domain comprising a CDR1 comprising SEQ ID NO: 5, a CDR2 comprising SEQ ID NO: 6, and a CDR3 comprising SEQ ID NO: 7.

In some ~~embodiment~~examples of any of the methods described herein, the antibody or the antigen-binding fragment thereof comprises a heavy chain variable domain comprising an amino acid sequence that is at least 80% identical to SEQ ID NO: 4 and a light chain variable domain comprising an amino acid sequence that is at least 80% identical to SEQ ID NO: 8.

In some ~~embodiment~~examples of any of the methods described herein, the antibody or the antigen-binding fragment thereof comprises a heavy chain variable domain comprising an amino acid sequence that is at least 90% identical to SEQ ID NO: 4 and a light chain variable domain comprising an amino acid sequence that is at least 90% identical to SEQ ID NO: 8.

In some ~~embodiment~~examples of any of the methods described herein, the antibody or the antigen-binding fragment thereof comprises a heavy chain variable domain comprising an amino acid sequence of SEQ ID NO: 4 and a light chain variable domain comprising an amino acid sequence of SEQ ID NO: 8.

In some ~~embodiment~~examples of any of the methods described herein, the antibody or the antigen-binding fragment is humanized.

In some ~~embodiment~~examples of any of the methods described herein, the antibody is an IgG1 antibody. In some ~~embodiment~~examples, the antibody or antigen-binding fragment is not a bispecific antibody, a bispecific T cell engager (BiTE), a chimeric antigen receptor (CAR), or an antibody drug conjugate (ADC), or a portion thereof.

In some ~~embodiment~~examples of any of the methods described herein, the one or more doses are independently administered to the subject at about 800 mg of the antibody or antigen-binding fragment to about 2,000 mg of the antibody or antigen-binding fragment.

In some ~~embodiment~~examples of any of the methods described herein, the one or more doses are independently administered to the subject at about 1,200 mg of the antibody or antigen-binding fragment to about 2,000 mg of the antibody or antigen-binding fragment.

In some ~~embodiment~~examples of any of the methods described herein, the one or more doses are independently administered to the subject at about 1,400 mg of the antibody or antigen-binding fragment to about 1,800 mg of the antibody or antigen-binding fragment.

In some ~~embodiment~~examples of any of the methods described herein, the one or more doses are independently administered to the subject at about 400 mg of the antibody or antigen-binding fragment.

In some ~~embodiment~~examples of any of the methods described herein, the one or more doses are independently administered to the subject at about 800 mg of the antibody or antigen-binding fragment.

In some ~~embodiment~~examples of any of the methods described herein, the one or more doses are administered to the subject at about 1,600 mg of the antibody or antigen-binding fragment.

In some ~~embodiment~~examples of any of the methods described herein, two or more doses of the antibody or antigen-binding fragment are administered to the subject.

In some ~~embodiment~~examples of any of the methods described herein, the two or more doses are administered to the subject at a frequency of between once a week and about once every four weeks.

In some ~~embodiment~~examples of any of the methods described herein, the two or more doses are administered to the subject at a frequency of about once a week.

In some ~~embodiment~~examples of any of the methods described herein, the two or more doses are administered to the subject at a frequency of about once every two weeks.

In some ~~embodiment~~examples of any of the methods described herein, the two or more doses are administered to the subject at a frequency of about once every three weeks.

In some ~~embodiment~~examples of any of the methods described herein, the two or more doses are administered to the subject at a frequency of about once every four weeks.

In some ~~embodiment~~examples of any of the methods described herein, each dose comprises about 800 mg of the antibody or antigen-binding fragment and is administered to the subject every 2 weeks.

In some ~~embodiment~~examples of any of the methods described herein, each dose comprises about 1600 mg of the antibody or antigen-binding fragment and is administered to the subject every 2 weeks.

In some ~~embodiment~~examples of any of the methods described herein, individual doses of the antibody or antigen-binding fragment are administered to the subject on day 1 and day 15 of a 28-day cycle.

In some ~~embodiment~~examples of any of the methods described herein, the doses of the antibody or antigen-binding fragment are administered to the subject for multiple 28-day cycles.

In some ~~embodiment~~examples of any of the methods described herein, the one or more doses comprise one or more induction doses that are administered to the subject during an induction phase and one or more maintenance doses that are administered to the subject during a maintenance phase after the one or more induction doses have been administered.

In some ~~embodiment~~examples of any of the methods described herein, one of the induction doses is administered to the subject about once a week for about 1-10 weeks.

In some ~~embodiment~~examples of any of the methods described herein, one of the induction doses is administered to the subject once a week for 8 weeks.

In some ~~embodiment~~examples of any of the methods described herein, one of the induction doses is administered 4 times within a 28-day cycle.

In some ~~embodiment~~examples of any of the methods described herein, one of the induction doses is administered 8 times within two 28-day cycles.

In some ~~embodiment~~examples of any of the methods described herein, one of the induction doses is independently administered on day 1, day 8, day 15 and day 22 for each of two 28-day cycles.

In some ~~embodiment~~examples of any of the methods described herein, each induction dose comprises about 100, 200, 400, 800, or 1600 mg of the antibody or antigen-binding fragment.

In some ~~embodiment~~examples of any of the methods described herein, each induction dose comprises about 800 mg of the antibody or antigen-binding fragment.

In some ~~embodiment~~examples of any of the methods described herein, each induction dose comprises about 1600 mg of the antibody or antigen-binding fragment.

In some ~~embodiment~~examples of any of the methods described herein, the one or more maintenance doses are administered once every 1-4 weeks after completion of the induction phase.

In some ~~embodiment~~examples of any of the methods described herein, one of the maintenance doses is administered once every two weeks.

In some ~~embodiment~~examples of any of the methods described herein, one of the maintenance doses is administered on day 1 and day 15 of a 28-day cycle.

In some ~~embodiment~~examples of any of the methods described herein, each maintenance dose comprises about 100, 200, 400, 800, or 1600 mg of the antibody or antigen-binding fragment.

In some ~~embodiment~~examples of any of the methods described herein, each maintenance dose comprises about 800 mg of the antibody or antigen-binding fragment.

In some ~~embodiment~~examples of any of the methods described herein, each maintenance dose comprises about 1600 mg of the antibody or antigen-binding fragment.

In some ~~embodiment~~examples of any of the methods described herein, the antibody or antigen-binding fragment is dosed q1wk during the induction phase for a total of 8 induction phase doses and dosed q2wk during the maintenance phase.

In some ~~embodiment~~examples of any of the methods described herein, each induction dose comprises about 100, 200, 400, or 1600 mg of the antibody or antigen-binding fragment; each maintenance dose comprises about 100, 200, 400, or 1600 mg of the antibody or antigen-binding fragment; one of the induction doses is administered on each of day 1, day 8, day 15 and day 22 for each of two 28-day cycles for a total of 8 induction doses during the induction phase; and one of the maintenance doses is administered on each of days 1 and day 15 of each of one or more subsequent cycles.

In some ~~embodiment~~examples of any of the methods described herein, each induction dose and each maintenance dose comprises about 800 or 1600 mg of the antibody or antigen-binding fragment.

In some ~~embodiment~~examples of any of the methods described herein, each induction dose and each maintenance dose comprises about 1600 mg of the antibody or antigen-binding fragment.

In some ~~embodiment~~examples of any of the methods described herein, the method further comprises administering one or more doses of dexamethasone to the subject.

In some ~~embodiment~~examples of any of the methods described herein, the one or more doses of dexamethasone are independently administered to the subject at a frequency of once a week.

In some ~~embodiment~~examples of any of the methods described herein, one of the doses of the antibody or antigen-binding fragment are administered at a frequency of about once every 1-4 weeks and the doses of dexamethasone are administered at a frequency of about once every 1-4 weeks.

In some ~~embodiment~~examples of any of the methods described herein, one of the doses of the antibody or antigen binding fragment are administered once every two weeks and one of the doses of dexamethasone is administered once every two weeks.

In some ~~embodiment~~examples of any of the methods described herein, one of the doses of the antibody or antigen binding fragment is administered once every two weeks and one of the doses of dexamethasone is administered once every week.

In some ~~embodiment~~examples of any of the methods described herein, one of the doses of the antibody or antigen binding fragment is administered on each of day 1 and day 15 of a 28-day cycle and one of the doses of dexamethasone is administered on each of day 1, day 8, day 15 and day 22 of the same 28-day cycle.

In some ~~embodiment~~examples of any of the methods described herein, one of the doses of the antibody or antigen-binding fragment is administered once a week during an induction phase with subsequent doses following the induction phase being administered once every two weeks during a maintenance phase; and one of the doses of dexamethasone is administered once every week.

In some ~~embodiment~~examples of any of the methods described herein, one of the doses of the antibody or antigen-binding fragment is administered once a week for 8 weeks during the induction phase and subsequent doses are administered once every two weeks during the maintenance phase; and one of the doses of dexamethasone is administered once every week.

In some ~~embodiment~~examples of any of the methods described herein, one of the doses of the antibody or antigen-binding fragment is administered on each of day 1, day 8, day 15, and day 22 of each of two 28-day cycles and then on each of day 1 and day 15 of subsequent 28-day cycles; and one of the doses of dexamethasone is administered on each of day 1, day 8, day 15, and day 22 of each of the 28-day cycles.

In some ~~embodiment~~examples of any of the methods described herein, when the antibody or antigen-binding fragment are administered on the same day then dexamethasone is administered about 1-3 hours before the antibody or antigen binding fragment is administered.

In some ~~embodiment~~examples of any of the methods described herein, each dose of the antibody or antigen-binding fragment is administered as an about 800 mg dose.

In some ~~embodiment~~examples of any of the methods described herein, each dose of the antibody or antigen-binding fragment is administered as an about 1600 mg dose.

In some ~~embodiment~~examples of any of the methods described herein, each dose of dexamethasone is administered as an about 20 to about 60 mg dose.

In some ~~embodiment~~examples of any of the methods described herein, each dose of dexamethasone is administered as an about 40 mg dose or an about 20 mg dose.

In some ~~embodiment~~examples of any of the methods described herein, each dose of the antibody or antigen-binding fragment is administered as an about 1600 mg dose, and wherein each dose of dexamethasone is administered as an about 40 mg dose.

In some ~~embodiment~~examples, the method further comprises administering one or more doses of an anti-CD38 antibody, or antigen-binding fragment thereof to the subject. In some ~~embodiment~~examples, the anti-CD38 antibody is daratumumab.

In some ~~embodiment~~examples, the one or more doses of the anti-CD38 antibody or antigen binding fragment thereof are independently administered to the subject at about 5 mg/kg (milligram per kilogram of body weight) to about 30 mg/kg. In some ~~embodiment~~examples, the one or more doses of the anti-CD38 antibody or antigen-binding fragment thereof are independently administered to the subject at about 10 mg/kg to about 20 mg/kg. In some ~~embodiment~~examples, the one or more doses of the anti-CD38 antibody or antigen-binding fragment thereof are independently administered to the subject at about 16 mg/kg.

In some ~~embodiment~~examples, two or more doses of the anti-CD38 antibody or antigen-binding fragment are administered to the subject. In some ~~embodiment~~examples, the two or more doses of the anti-CD38 antibody or antigen binding fragment thereof are administered to the subject at a frequency of about once a week to about once every four weeks. In some ~~embodiment~~examples, the two or more doses of the anti-CD38 antibody or antigen-binding fragment thereof are administered to the subject at a frequency of about once a week. In some ~~embodiment~~examples, the two or more doses of the anti-CD38 antibody or antigen-binding fragment thereof are administered to the subject at a frequency of about once every two weeks or once every three weeks. In some ~~embodiment~~examples, the two or more doses of the anti-CD38 antibody or antigen-binding fragment thereof are administered to the subject at a frequency of about once every four weeks. In some ~~embodiment~~examples, the anti-CD38 antibody or antigen-binding fragment thereof are administered to the subject on day 1, day 8, day 15, and day 22 for 28-day cycles.

In some ~~embodiment~~examples, two or more doses of the anti-CD38 antibody or antigen-binding fragment thereof are administered to the subject at a frequency of about once every week during

a first phase; two or more doses of the anti-CD38 antibody or antigen binding-fragment thereof are administered to the subject at a frequency of about once every two weeks to about once every three weeks during a second phase; and two or more doses of the anti-CD38 antibody or antigen binding fragment thereof are administered to the subject at a frequency of about once every four weeks during a third phase.

In some ~~embodiment~~examples, the first phase is about 6 weeks to about 10 weeks. In some ~~embodiment~~examples, the first phase is about 8 weeks or about 9 weeks. In some ~~embodiment~~examples, the second phase is about 10 weeks to about 20 weeks.

In some ~~embodiment~~examples, 8 doses of the anti-CD38 antibody or antigen-binding fragment thereof are administered to the subject at a frequency of about once every two weeks during the second phase. In some ~~embodiment~~examples, 5 doses of the anti-CD38 antibody or antigen-binding fragment thereof are administered to the subject at a frequency of about once every three weeks during the second phase.

In some ~~embodiment~~examples, multiple doses of the anti-CD38 antibody or antigen-binding fragment thereof are administered to the subject at a frequency of about once every four weeks during the third phase until disease progression.

In some ~~embodiment~~examples, the method further comprises administering one or more doses of an immunomodulatory drug. In some ~~embodiment~~examples, the immunomodulatory drug is an immunomodulatory imide drug (IMiD). In some ~~embodiment~~examples, the immunomodulatory drug is lenalidomide or pomalidomide.

In some ~~embodiment~~examples, the immunomodulatory drug is pomalidomide.

In some ~~embodiment~~examples, the one or more doses of the immunomodulatory drug are independently administered to the subject at a frequency of about once per day to about once per week. In some ~~embodiment~~examples, the one or more doses of the immunomodulatory drug are independently administered to the subject once per day. In some ~~embodiment~~examples, the one or more doses of the immunomodulatory drug are independently administered to the subject once per day on Days 1-21 of repeated 28-day cycles.

In some ~~embodiment~~examples, each dose of the immunomodulatory drug is about 1 mg to about 10 mg. In some ~~embodiment~~examples, each dose of the immunomodulatory drug is about 2 mg to about 4 mg. In some ~~embodiment~~examples, each dose of the immunomodulatory drug is about 4 mg.

In some ~~embodiment~~examples, when a dose of the immunomodulatory drug and a dose of the antibody or antigen-binding fragment that specifically binds to BCMA are administered on the same day, the dose of the immunomodulatory drug is administered about 1 to about 3 hours before the dose of the antibody or antigen-binding fragment that specifically binds to BCMA.

In some ~~embodiment~~examples, the antibody or antigen-binding fragment that specifically binds to BCMA is administered to the subject on day 1 and day 15 of a 28-day cycle, dexamethasone is administered to the subject on day 1, 8, 15, and 22 of the 28-day cycle, and pomalidomide is administered to the subject on days 1-21 of the 28-day cycle.

In some ~~embodiment~~examples, one of the induction doses of the antibody or antigen-binding fragment that specifically binds to BCMA is administered on each of day 1, day 8, day 15 and day 22 for two 28-day cycles for a total of 8 induction doses during the induction phase; and one of the maintenance doses of the antibody or antigen-binding fragment that specifically binds to BCMA is administered on each of days 1 and day 15 of each of one or more subsequent 28-day cycles in the maintenance phase;

In some ~~embodiment~~examples, dexamethasone is administered to the subject on each of day 1, 8, 15, and 22 of each 28-day cycle in the induction phase and the maintenance phase. In some ~~embodiment~~examples, pomalidomide is administered to the subject on days 1-21 of each 28-day cycle in the induction phase and the maintenance phase.

In some ~~embodiment~~examples, when a dose of dexamethasone and a dose of the antibody or antigen-binding fragment are administered on the same day or a dose of pomalidomide and a dose of the antibody or antigen-binding fragment are administered on the same day, the dose of dexamethasone or the dose of pomalidomide is administered about 1 to about 3 hours before the dose of the antibody or antigen-binding fragment.

In some ~~embodiment~~examples, the method further comprises administering one or more doses of a gamma-secretase inhibitor to the subject. In some ~~embodiment~~examples, the gamma-secretase inhibitor is Semagacestat (LY450139), RO4929097, MK-0752, Avagacestat (BMS-708163), BMS-986115, Nirogacestat (PF-03084014), Crenigacestat (LY3039478), BMS-906024, DAPT (GSI-IX), Dibenzazepine (YO-01027), LY411575, L-685458, NGP 555, MDL-28170, or Itanapraced (CHF 5074). Some of these gamma-secretase inhibitors are described in e.g. WO2019094626A1, US 9914774, U.S. 6756511, US 6890956, US 6984626, US 7049296, US 7101895, US 7138400, US 7144910, US 7183303, US 8377886, WO 2002/40451A2, US7468365B2, US20160354382,

US2020179511A1, US2019367628A1, US2020085839A1, US10590087, US2020171020A1, US662510A, US4434171A, US2019367628A1, US2019367628A1, US 7244739, US2020087623A1, US10307388B2, and PubChem of the NCBI website; each of which is incorporated herein by the reference in its entirety.

In some ~~embodiment~~examples of any of the methods described herein, each dose of the antibody or antigen-binding fragment is administered by systemic administration.

In some ~~embodiment~~examples of any of the methods described herein, the systemic administration is by intravenous administration.

In some ~~embodiment~~examples of any of the methods described herein, at least the initial dose of the antibody or antigen-binding fragment is administered to the subject using step-wise infusion.

In some ~~embodiment~~examples of any of the methods described herein, the step-wise infusion is performed using an infusion rate of about 50 mg/hour to about 400 mg/hour.

In some ~~embodiment~~examples of any of the methods described herein, the step-wise infusion, the infusion rate is increased every 30 minutes.

In some ~~embodiment~~examples of any of the methods described herein, the step-wise infusion, the infusion rate is increased no more than two-fold every 30 minute.

In some ~~embodiment~~examples of any of the methods described herein, the subject is a human subject.

In some ~~embodiment~~examples of any of the methods described herein, the subject has previously been diagnosed as having multiple myeloma.

In some ~~embodiment~~examples of any of the methods described herein, the subject has been diagnosed as having relapsed or refractory multiple myeloma.

In some ~~embodiment~~examples of any of the methods described herein, the subject was previously administered one or more therapeutic agents or treatments for multiple myeloma.

In some ~~embodiment~~examples of any of the methods described herein, the previously administered one or more therapeutic agents or treatments for multiple myeloma were unsuccessful.

In some ~~embodiment~~examples of any of the methods described herein, the subject has previously been administered at least one of a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 antibody, or cannot tolerate the foregoing.

In some ~~embodiment~~examples of any of the methods described herein, the subject has previously been administered therapeutic agents include all three of a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 antibody, or cannot tolerate the foregoing.

In some ~~embodiment~~examples of any of the methods described herein, the subject has previously been administered at least 3 prior lines of anti-myeloma therapy and is refractory to at least one therapeutic agent in each of the following classes: a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 antibody.

In some ~~embodiment~~examples of any of the methods described herein, the subject satisfies 1, 2 or all 3 of the following criteria prior to initiating treatment: serum monoclonal paraprotein (M-protein) level of ≥ about 0.5 g/dL, urine M-protein level ≥ about 200mg/24 hr, and serum immunoglobulin free light chain ≥ about10 mg/dL and abnormal serum immunoglobulin kappa lambda free light chain ratio.

In some ~~embodiment~~examples of any of the methods described herein, the method results in a steady-state concentration of the antibody, or antigen-binding fragment thereof, in the serum of the subject of about 1 µg/mL to about 200 µg/mL.

In some ~~embodiment~~examples of any of the methods described herein, the method results in a steady-state concentration of free light chain (FLC) in the serum of the subject of less than about 50 mg/dL.

In some ~~embodiment~~examples, the subject has received at least two prior lines of anti-myeloma therapy (e.g., including at least 2 consecutive cycles of lenalidomide and a proteosome inhibitor (e.g., given separately or in combination)), and has documented IMWG (International Myeloma Working Group) disease progression on or within 60 days of completion of the two prior lines of anti-myeloma therapy.

In some ~~embodiment~~examples of any of the methods described herein, one or more therapeutic effects in the subject is improved after administration of the antibody-drug conjugate relative to a baseline.

In some ~~embodiment~~examples of any of the methods described herein, the one or more therapeutic effects is selected from the group consisting of: objective response rate, complete response rate, duration of response, duration of complete response, time to response, progression free survival, and overall survival.

In some ~~embodiment~~examples of any of the methods described herein, the objective response rate is at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 60%, at least about 70%, or at least about 80%.

In some ~~embodiment~~examples of any of the methods described herein, the subject exhibits progression-free survival of at least about 1 month, at least about 2 months, at least about 3 months, at least about 4 months, at least about 5 months, at least about 6 months, at least about 7 months, at least about 8 months, at least about 9 months, at least about 10 months, at least about 11 months, at least about 12 months, at least about eighteen months, at least about two years, at least about three years, at least about four years, or at least about five years.

In some ~~embodiment~~examples of any of the methods described herein, the subject exhibits overall survival of at least about 1 month, at least about 2 months, at least about 3 months, at least about 4 months, at least about 5 months, at least about 6 months, at least about 7 months, at least about 8 months, at least about 9 months, at least about 10 months, at least about 11 months, at least about 12 months, at least about eighteen months, at least about two years, at least about three years, at least about four years, or at least about five years.

In some ~~embodiment~~examples of any of the methods described herein, the duration of response or the duration of complete response to the treatment is at least about 1 month, at least about 2 months, at least about 3 months, at least about 4 months, at least about 5 months, at least about 6 months, at least about 7 months, at least about 8 months, at least about 9 months, at least about 10 months, at least about 11 months, at least about 12 months, at least about eighteen months, at least about two years, at least about three years, at least about four years, or at least about five years.

In one aspect, the present disclosure refers to a kit comprising: (a) one or more doses of a pharmaceutical composition comprising (i) an antibody, or antigen binding fragment thereof, that specifically binds to a B cell maturation antigen (BCMA), and (ii) a pharmaceutically acceptable carrier, wherein the antibody or antigen binding fragment thereof, comprises: a heavy chain variable region comprising a CDR1 comprising SEQ ID NO: 1, a CDR2 comprising SEQ ID NO: 2, and a CDR3 comprising SEQ ID NO: 3, and a light chain variable domain comprising a CDR1 comprising SEQ ID NO: 5, a CDR2 comprising SEQ ID NO: 6, and a CDR3 comprising SEQ ID NO: 7; and optionally (b) instructions for performing any of the uses described herein.

Also provided are kits comprising: (a) one or more doses of a pharmaceutical composition comprising (i) an antibody, or antigen binding fragment thereof, that specifically binds to a B cell maturation antigen (BCMA), and (ii) a pharmaceutically acceptable carrier, wherein the antibody or antigen binding fragment thereof, comprises: a heavy chain variable region comprising a CDR1 comprising SEQ ID NO: 1, a CDR2 comprising SEQ ID NO: 2, and a CDR3 comprising SEQ ID NO: 3, and a light chain variable domain comprising a CDR1 comprising SEQ ID NO: 5, a CDR2 comprising SEQ ID NO: 6, and a CDR3 comprising SEQ ID NO: 7, and (b) instructions for performing any of the methods described herein.

Also provided herein are methods of treating a subject having multiple myeloma, the method including administering to the subject one or more doses of a pharmaceutical composition comprising (i) an antibody, or antigen-binding fragment thereof, that specifically binds to a B cell maturation antigen (BCMA), and (ii) a pharmaceutically acceptable carrier.

In some ~~embodiment~~examples of any of the methods described herein, the multiple myeloma is relapsed or refractory multiple myeloma (RRMM). In some ~~embodiment~~examples, the antibody, or antigen-binding fragment thereof comprises: a heavy chain variable region comprising a CDR1 comprising SEQ ID NO: 1, a CDR2 comprising SEQ ID NO: 2, and a CDR3 comprising SEQ ID NO: 3, and a light chain variable domain comprising a CDR1 comprising SEQ ID NO: 5, a CDR2 comprising SEQ ID NO: 6, and a CDR3 comprising SEQ ID NO: 7.

In some ~~embodiment~~examples, the antibody is an IgG1 antibody. In some ~~embodiment~~examples, one or more doses of about 1600 mg of the antibody, or antigen-binding fragment thereof, is independently administered to the subject at a frequency of every two weeks. In some ~~embodiment~~examples, one or more doses of about 800 mg of the antibody, or antigen-binding fragment thereof, is independently administered to the subject at a frequency of every week. In some ~~embodiment~~examples, about 1-2 induction doses of about 1600 mg of the antibody, or antigen-binding fragment thereof, is independently administered to the subject at a frequency of every week, followed by one or more maintenance doses of about 1600 mg of the antibody, or antigen-binding fragment thereof, independently administered to the subject at a frequency of every two weeks. In some ~~embodiment~~examples, about 1-2 induction doses of about 800 mg of the antibody, or antigen-binding fragment thereof, is independently administered to the subject at a frequency of every week, followed by one or more maintenance doses of about 1600 mg of the antibody, or antigen-binding fragment thereof, independently administered to the subject at a frequency of every two weeks. In some ~~embodiment~~examples, a dose of about 40 mg of dexamethasone is administered to the subject about 1 to about 3 hours prior to the administration of each dose of the antibody, or antigen-binding fragment thereof.

In some ~~embodiment~~examples, the subject was previously administered one or more therapeutic agents or treatments for multiple myeloma. The one or more previously administered therapeutic agents or treatments for multiple myeloma include, but are not limited to, a proteasome inhibitor (PI), an immunomodulatory drug (IMiD), and an anti-CD38 antibody. In some ~~embodiment~~examples, the previously administered therapeutic agents or treatments for multiple myeloma were not

effective in treating the multiple myeloma. In some ~~embodiment~~examples, the subject has one or more of: a serum monoclonal paraprotein (M-protein) level of ≥ about 0.5 g/dL, a urine M-protein level of ≥ about 200 mg/24 hours, a serum immunoglobulin free light chain ≥ about 10 mg/dL, and an abnormal serum immunoglobulin kappa to lambda free light chain ratio.

Also provided herein are kits that comprise or consist of (a) one or more doses of a pharmaceutical composition comprising (i) an antibody, or antigen-binding fragment thereof, that specifically binds to a B cell maturation antigen (BCMA), and (ii) a pharmaceutically acceptable carrier, wherein the antibody or antigen-binding fragment thereof, comprises: a heavy chain variable region comprising a CDR1 comprising SEQ ID NO: 1, a CDR2 comprising SEQ ID NO: 2, and a CDR3 comprising SEQ ID NO: 3, and a light chain variable domain comprising a CDR1 comprising SEQ ID NO: 5, a CDR2 comprising SEQ ID NO: 6, and a CDR3 comprising SEQ ID NO: 7; and optionally (b) instructions for performing a treatment method as described herein.

In some ~~embodiment~~examples, the kit further comprises one or more doses of dexamethasone, one or more doses of an immunomodulatory imide drug, one or more doses of a gamma-secretase inhibitor, and/or one or more doses of an anti-CD38 antibody or antigen binding fragment thereof.

In some ~~embodiment~~examples, the kit further comprises one or more doses of dexamethasone.

In some ~~embodiment~~examples, the kit further comprises one or more doses of an immunomodulatory imide drug.

In some ~~embodiment~~examples, the kit further comprises one or more doses of dexamethasone and one or more doses of an immunomodulatory imide drug.

In some ~~embodiment~~examples, the kit further comprises one or more doses of a gamma-secretase inhibitor.

In some ~~embodiment~~examples, the kit further comprises one or more doses of an anti-CD38 antibody.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this ~~invention~~disclosure belongs. Methods and materials are described herein for use in the present ~~invention~~disclosure; other, suitable methods and materials known in the art can also be used. The materials, methods, and examples are illustrative only and not intended to be limiting. All publications, patent

applications, patents, sequences, database entries, and other references mentioned herein are incorporated by reference in their entirety. In case of conflict, the present specification, including definitions, will control.

Other features and advantages of the ~~invention~~disclosure will be apparent from the following detailed description and figures, and from the claims.

DESCRIPTION OF DRAWINGS

FIG. 1A is a graph showing the mean serum concentration of the SEA-BCMA antibody over time in subjects administered different doses of SEA-BCMA.

FIG. 1B shows the results of the pharmacokinetic analysis of SEA-BCMA depicted in **FIG. 1A**.

FIG. 2A is a schematic illustration showing the detection of free SEA-BCMA using an in vitro cell binding capacity assay.

FIG. 2B shows the standard curves generated using the assay depicted in **FIG. 2A**.

FIG. 3A is a graph showing the percentage of membrane-bound BCMA in an in vitro membrane BCMA assay performed using serum from subjects administered 100 mg, 200 mg, or 400 mg doses of SEA-BCMA, with each line corresponding to a different subject.

FIG. 3B is a graph showing the percentage of membrane-bound BCMA in an in vitro membrane BCMA assay performed using serum from subjects administered 800 mg doses of SEA-BCMA, with each line corresponding to a different subject.

FIG. 3C is a graph showing the percentage of membrane-bound BCMA in an in vitro membrane BCMA assay performed using serum from subjects administered 1600 mg doses of SEA-BCMA.

FIG. 4 is a bar graph showing the binding of membrane BCMA on the surface of malignant plasma cells.

FIG. 5 shows previous treatments administered to one patient and results after treatment with SEA-BCMA.

FIG. 6A is a graph showing serum free light chain (sFLC) levels in a patient (Patient A) after administration of a 1600 mg dose of SEA-BCMA.