CLAIMS

1. Use of an antagonist of Neutrokine-alpha for the preparation of a medicament for treating a patient with an autoimmune disease that has an ANA titer ≥ 1:80 or ≥ 30 IU/mL of anti-dsDNA antibodies in his/her blood plasma or serum, wherein said antagonist is formulated for administration to said patient in a therapeutically effective amount.

2. The use of claim 1, wherein said autoimmune disease is systemic lupus erythematosus (SLE).

3. The use of claim 1, wherein the autoimmune disease is rheumatoid arthritis, Sjagren's syndrome, scleroderma, polymyositis, dermatomyositis, Felty's syndrome, mixed connective tissue disease, Raynaud's syndrome, or juvenile chronic arthritis.

4. The use of claims 1 to 3, wherein said antagonist of Neutrokinealpha is administered after making a determination that the patient has an ANA titer ≥ 1:80 or 30 IU/mL of anti-dsDNA antibodies in his/her blood plasma or serum.

5. Use of an antagonist of Neutrokine-alpha for the preparation of a medicament for treating a patient with systemic lupus erythematosus, wherein said antagonist is formulated for administration in a therapeutically effective amount to said patient after making a determination that said patient has an of ANA titer ≥ 1:80 or ≥ 30 IU/mL of anti-dsDNA antibodies in his/her blood plasma or serum.

6. The use of claim 5, wherein said antagonist of Neutrokine-alpha is administered after making a determination that the patient has at least one characteristic selected from the group consisting of:

(a) a SELENA SLEDAI score ≥ 6;

(b) a depressed level of C3 complement factor in his/her blood plasma or serum;

(c) a depressed level of C4 complement factor in his/her blood plasma or serum;

(d) the patient is receiving ≥ 7.5 milligrams/day of prednisone; and

(e) the patient is receiving or had previously received immunosuppressant therapy for the treatment of lupus-related symptoms.

7. The use of claim 5 or claim 6, wherein said antagonist of Neutrokinealpha is administered after making a determination that the patient has less than 90 milligrams/deciliter of C3 complement factor in his/her blood plasma or serum.

8. The use of any one of claims 5 to 6, wherein said antagonist of Neutrokinealpha is administered after making a determination that the patient has less than 16 milligrams/deciliter of C4 complement factor in his/her blood plasma or serum.

9. The use of any one of claims 4 to 8, wherein the determination is to be made on the basis of the patient's medical record or on the basis of laboratory tests.

10. The use of any one of claims 1 to 9, wherein the antagonist of Neutrokinealpha is administered in combination with an anti-CD20 antibody.

11. The use of any one of claims 1 to 10, wherein said patient has an ANA titer ≥ 1:80 and ≥ 30 IU/mL of anti-dsDNA antibodies in his/her blood plasma or serum.

12. The use of any one of claims 1 to 11, wherein said antagonist is an anti-Neutrokine-alpha antibody.

13. The use of claim 12, wherein the antibody comprises the amino acid sequences of a set of VH and VL domains selected from the group consisting of:

(a) the VH domain and the VL domain of SEQ ID NO:13;
(b) the VH domain and the VL domain of SEQ ID NO: 14;
(c) the VH domain and the VL domain of SEQ ID NO: 15;
(d) the VH domain and the VL domain of SEQ ID NO:16;
(e) the VH domain and the VL domain of SEQ ID NO: 17;
(f) the VH domain and the VL domain of SEQ ID NO: 18;
(g) the VH domain of SEQ ID NO:19 and the VL domain of SEQ ID NO:20; and
(h) the VH domain of SEQ ID NO:21 and the VL domain of SEQ ID NO:22.

14. The use of any one of claims 1 to 11, wherein said antagonist is a protein comprising the Neutrokine-alpha binding domain of TACI (SEQ ID NO:6), the Neutrokinealpha binding domain of BCMA (SEQ ID NO:8), the Neutrokine-alpha binding domain of BAFF-R (SEQ ID NO: 10) or a variant of the BAFF-R Neutrokine-alpha binding domain having the amino acid sequence of amino acid residues 2-70 of SEQ ID NO:26.

15. The use of any one of claims 1 to 11, wherein said antagonist is a Neutrokine-alpha-binding peptide, a peptibody, a Neutrokine-alpha protein variant or an anti-Neutrokine-alpha receptor antibody.

16. The use of claim 15, wherein the Neutrokine-alpha protein variant acts as a dominant negative.

17. The use of claim 13, wherein the antibody comprises the VH domain and the VL domain of SEQ ID NO:17.

18. The use of any one of claims 12, 13 and 17, wherein the antibody is radiolabelled.

19. The use of any one of claims 12, 13, 17 and 18, wherein the antibody neutralizes B Lymphocyte Stimulator protein (BLyS).

20. The use of any one of claims 12, 13, 17 and 18, wherein the antibody inhibits BLyS from binding to its receptor.

21. The use of any one of claims 12, 13, 17 and 18, wherein the antibody inhibits B cell proliferation.

22. The use of any one of claims 12, 13, 17 and 18, wherein the antibody inhibits B cell survival.

23. The use of any one of claims 12, 13, 17 and 18, wherein the antibody inhibits immunoglobulin production.

What is claimed is:

1. A method of treating a patient that has an ANA titer ≥ 1:80 or ≥ 30 IU/mL of anti-dsDNA antibodies in his/her blood plasma or serum comprising administering a therapeutically effective amount of an antagonist of Neutrokine-alpha.

2. The method of claim 1 wherein the patient has an ANA titer ≥ 1:80 and ≥ 30 IU/mL of anti-dsDNA antibodies in his/her blood plasma or serum.

3. The method of claim 1 wherein the antagonist of Neutrokine-alpha is administered in combination with an anti-CD20 antibody

4. The method of claim 1 which comprises making a determination, prior to administering the antagonist of Neutrokine-alpha, that the patient has an ANA titer ≥ 1:80 or ≥ 30 IU/mL of anti-dsDNA antibodies in his/her blood plasma or serum.

5. The method of claim 4 wherein the determination is made on the basis of the patient's medical record.

6. The method of claim 4 wherein the determination is made on the basis of laboratory tests.

7. The method of claim 1 wherein the antagonist of Neutrokine-alpha is an anti-Neutrokine-alpha antibody.

8. The method of claim 1 wherein the antagonist of Neutrokine-alpha is a protein comprising the Neutrokine-alpha binding domain of TACI (SEQ ID NO:6).

9. The method of claim 1 wherein the antagonist of Neutrokine-alpha is a protein comprising the Neutrokine-alpha binding domain of BCMA (SEQ ID NO:8).

10. The method of claim 1 wherein the antagonist of Neutrokine-alpha is a protein comprising the Neutrokine-alpha binding domain of BAFF-R (SEQ ID NO:10) or a variant of the BAFF-R Neutrokine-alpha binding domain having the amino acid sequence of amino acid residues 2-70 of SEQ ID NO:26.

11. The method of claim 1 wherein the antagonist of Neutrokine-alpha is a Neutrokine-alpha-binding peptide, a peptibody, a Neutrokine-alpha protein variant or an anti-Neutrokine-alpha receptor antibody.

12. The method of claim 11 wherein the Neutrokine-alpha protein variant acts as a dominant negative.

13. The method of claim 1 wherein the patient has an autoimmune disease.

14. The method of claim 13 wherein the autoimmune disease is systemic lupus erythematosus (SLE).

15. The method of claim 14 wherein the antagonist of Neutrokine-alpha is administered in combination with an anti-CD20 antibody.

16. The method of claim 13 wherein the autoimmune disease is rheumatoid arthritis, Sjögren's syndrome, scleroderma, polymyositis, dermatomyositis, Felty's syndrome, mixed connective tissue disease, Raynaud's syndrome, or juvenile chronic arthritis.

17. The method of claim 7 wherein the antibody comprises the amino acid sequences of a set of VH and VL domains selected from the group consisting of:

(a) the VH domain and the VL domain of SEQ ID NO:13;
(b) the VH domain and the VL domain of SEQ ID NO:14;
(c) the VH domain and the VL domain of SEQ ID NO:15;
(d) the VH domain and the VL domain of SEQ ID NO:16;
(e) the VH domain and the VL domain of SEQ ID NO:17;
(f) the VH domain and the VL domain of SEQ ID NO:18;
(g) the VH domain of SEQ ID NO:19 and the VL domain of SEQ ID NO:20; and
(h) the VH domain of SEQ ID NO:21 and the VL domain of SEQ ID NO:22.

18. A method of treating a patient with systemic lupus erythematosus comprising:

(a) making a determination that the patient has an ANA titer ≥ 1:80 or ≥ 30 IU/mL of anti-dsDNA antibodies in his/her blood plasma or serum; and

(b) administering a therapeutically effective amount of an antagonist of Neutrokine-alpha to said patient after making said determination.

19. The method of claim 18 wherein the patient has ANA titer ≥ 1:80 and ≥ 30 IU/mL of anti-dsDNA antibodies in his/her blood plasma or serum.

20. The method of claim 18 wherein the antagonist of Neutrokine-alpha is administered in combination with an anti-CD20 antibody.

21. The method of claim 18 which also comprises making a determination, prior to administering the antagonist of Neutrokine-alpha, that the patient has at least one characteristic selected from the group consisting of:

(a) a SELENA SLEDAI score ≥ 6.
(b) a depressed level of C3 complement factor in his/her blood plasma or serum;
(c) a depressed level of C4 complement factor in his/her blood plasma or serum;
(d) the patient is receiving ≥7.5 milligrams/day of prednisone; and
(e) the patient is receiving or had previously received immunosuppressant therapy for the treatment of lupus-related symptoms.

22. The method of claim 21 which comprises making a determination that the patient has a SELENA SLEDAI score greater ≥ 6 prior to administering the antagonist of Neutrokine-alpha.

23. The method of claim 21 which comprises making a determination that the patient has less than 90 milligrams/deciliter of C3 complement factor in his/her blood plasma or serum prior to administering the antagonist of Neutrokine-alpha.

24. The method of claim 21 which comprises making a determination that the patient has less than 16 milligrams/deciliter of C4 complement factor in his/her blood plasma or serum prior to administering the antagonist of Neutrokine-alpha.

25. The method of claim 21 which comprises making a determination that the patient is receiving ≥7.5 milligrams/day of prednisone prior to administering the antagonist of Neutrokine-alpha.

26. The method of claim 21 which comprises making a determination that the patient is receiving or had previously received immunosuppressant therapy for the treatment of lupus-related symptoms prior to administering the antagonist of Neutrokine-alpha.

27. The method of claim 18 wherein the determination is made on the basis of the patient's medical record.

28. The method of claim 18 wherein the determination is made on the basis of laboratory tests.

29. The method of claim 18 wherein the antagonist of Neutrokine-alpha is an anti-Neutrokine-alpha antibody.

30. The method of claim 18 wherein the antagonist of Neutrokine-alpha is a protein comprising the Neutrokine-alpha binding domain of TACI (SEQ ID NO:6).

31. The method of claim 18 wherein the antagonist of Neutrokine-alpha is a protein comprising the Neutrokine-alpha binding domain of BCMA (SEQ ID NO:8).

32. The method of claim 18 wherein the antagonist of Neutrokine-alpha is a protein comprising the Neutrokine-alpha binding domain of BAFF-R (SEQ ID NO:10) or a variant of the BAFF-R Neutrokine-alpha binding domain having the amino acid sequence of amino acid residues 2-70 of SEQ ID NO:26

33. The method of claim 18 wherein the antagonist of Neutrokine-alpha is a Neutrokine-alpha-binding peptide, a peptibody, a Neutrokine-alpha protein variant or an anti-Neutrokine-alpha receptor antibody.

34. The method of claim 33 wherein the Neutrokine-alpha protein variant acts as a dominant negative.

35. A method of reducing the frequency or quantity of corticosteroid administered to a patient with systemic lupus erythematosus comprising administering a therapeutically effective amount of an antagonist of Neutrokine-alpha to said patient.

36. The method of claim 35 which also comprises making a determination, prior to administering the antagonist of Neutrokine-alpha, that the patient has at least one characteristic selected from the group consisting of:

(a) an ANA titer ≥ 1:80;

(b) ≥ 30 IU/mL of anti-dsDNA antibodies in his/her blood plasma or serum;

(c) a SELENA SLEDAI score ≥ 6;

(d) a depressed level of C3 complement factor in his/her blood plasma or serum;

(e) a depressed level of C4 complement factor in his/her blood plasma or serum;

(f) the patient is receiving ≥7.5 milligrams/day of prednisone; and

(g) the patient is receiving or had previously received immunosuppressant therapy for the treatment of lupus-related symptoms.

37. The method of claim 36 which comprises making a determination that the patient has an ANA titer ≥ 1:80.

38. The method of claim 36 which comprises making a determination that the patient has ≥ 30 IU/mL of anti-dsDNA antibodies in his/her blood plasma or serum.

39. The method of claim 36 which comprises making a determination that the patient has an ANA titer ≥ 1:80 and ≥ 30 IU/mL of anti-dsDNA antibodies in his/her blood plasma or serum.

40. The method of claim 36 which comprises making a determination that the patient has a SELENA SLEDAI score greater ≥ 6 prior to administering the antagonist of Neutrokine-alpha.

41. The method of claim 36 which comprises making a determination that the patient has less than 90 milligrams/deciliter of C3 complement factor in his/her blood plasma or serum prior to administering the antagonist of Neutrokine-alpha.

42. The method of claim 36 which comprises making a determination that the patient has less than 16 milligrams/deciliter of C4 complement factor in his/her blood plasma or serum prior to administering the antagonist of Neutrokine-alpha.

43. The method of claim 36 which comprises making a determination that the patient is receiving ≥7.5 milligrams/day of prednisone prior to administering the antagonist of Neutrokine-alpha.

44. The method of claim 36 which comprises making a determination that the patient is receiving or had previously received immunosuppressant therapy for the treatment of lupus-related symptoms prior to administering the antagonist of Neutrokine-alpha.

45. The method of claim 36 wherein the determination is made on the basis of the patient's medical record.

46. The method of claim 36 wherein the determination is made on the basis of laboratory tests.

47. The method of claim 35 wherein the antagonist of Neutrokine-alpha is an anti-Neutrokine-alpha antibody.

48. The method of claim 35 wherein the antagonist of Neutrokine-alpha is a protein comprising the Neutrokine-alpha binding domain of TACI (SEQ ID NO:6).

49. The method of claim 35 wherein the antagonist of Neutrokine-alpha is a protein comprising the Neutrokine-alpha binding domain of BCMA (SEQ ID NO:8).

50. The method of claim 35 wherein the antagonist of Neutrokine-alpha is a protein comprising the Neutrokine-alpha binding domain of BAFF-R (SEQ ID NO:10) or a variant of the BAFF-R Neutrokine-alpha binding domain having the amino acid sequence of amino acid residues 2-70 of SEQ ID NO:26.

51. The method of claim 35 wherein the antagonist of Neutrokine-alpha is a Neutrokine-alpha-binding peptide, a peptibody, a Neutrokine-alpha protein variant or an anti-Neutrokine-alpha receptor antibody.

52. The method of claim 51 wherein the Neutrokine-alpha protein variant acts as a dominant negative.

53. The method of claim 35 wherein the corticosteroid is selected from the group consisting of prednisone, prednisolone, hydrocortisone, methylprednisolone and dexamethasone.

54. The method of claim 35 wherein the corticosteroid is prednisone.

55. The method of claim 54 wherein the quantity of prednisone administered to a patient is reduced by at least 25% to $\leq$ 7.5 milligrams/day.

56. A method of determining if a lupus patient is responding to medical treatment comprising:

(a) determining the patient's SELENA SLEDAI, BILAG and PGA score prior to administration of medical treatment;

(b) administering the medical treatment; and

(c) determining the patient's SELENA SLEDAI, BILAG and PGA score following the administration of the medical treatment;

wherein the patient is considered to have responded to medical treatment if the SELENA SLEDAI score determined in step (c) is 4 or more points less than the SELENA SLEDAI score determined in step (a), the BILAG index score determined in step (c) does not include a new BILAG A organ domain score or 2 new BILAG B organ domain scores compared to the BILAG score determined in step (a), and the PGA score determined in step (c) is < 0.3 point higher than the PGA score determined in step (a).

57. The method of claim 56 wherein the medical treatment is a pharmaceutical composition comprising an antagonist of Neutrokine-alpha.

58. The method of claim 56 wherein the antagonist of Neutrokine-alpha is an anti-Neutrokine-alpha antibody.

59. The method of claim 56wherein the antagonist of Neutrokine-alpha is a protein comprising the Neutrokine-alpha binding domain of TACI (SEQ ID NO:6).

60. The method of claim 56 wherein the antagonist of Neutrokine-alpha is a protein comprising the Neutrokine-alpha binding domain of BCMA (SEQ ID NO:8).

61. The method of claim 56 wherein the antagonist of Neutrokine-alpha is a protein comprising the Neutrokine-alpha binding domain of BAFF-R (SEQ ID NO:10) or a variant of the BAFF-R

Neutrokine-alpha binding domain having the amino acid sequence of amino acid residues 2-70 of SEQ ID NO:26.

62. The method of claim 56 wherein the antagonist of Neutrokine-alpha is a Neutrokine-alpha-binding peptide, a peptibody, a Neutrokine-alpha protein variant or an anti-Neutrokine-alpha receptor antibody.

63. The method of claim 62 wherein the Neutrokine-alpha protein variant acts as a dominant negative.

64. An aqueous pharmaceutical formulation comprising a therapeutically effective amount of an antibody, a buffer in an amount from about 5 mM to about 50 mM, NaCl in an amount from about 150 mM to about 500 mM, a surfactant in an amount from about 0.003% to about 0.05%, with a pH from about 5.5 to about 6.5.

65. The formulation of claim 64 wherein the antibody is a human IgG1/λ antibody, the buffer is 10 mM histidine, the surfactant is polysorbate 80 in an amount of 0.01% w/v, the NaCl is 150mM and wherein the formulation has a pH of 6.0.

66. The formulation of claim 65 which is stable at a temperature of about 2-8° C for at least one year.

67. The formulation of claim 65 which is stable at a temperature of about 2-8° C for at least two years.

68. The formulation of claim 65 wherein the antibody is present in an amount of 100 mg/ml.

69. The aqueous pharmaceutical formulation of claim 64 comprising 100 mg/ml IgG1/λ antibody, 0.74 mg/ml L-histidine, 1.1 mg/ml L-histidine monohydrochloride, 8.8 mg/ml NaCl and 0.1 mg/ml polysorbate 80 and wherein the formulation has a pH of 6.0.