

CLAIMS

1. A unit dose for subcutaneous administration comprising more than (>)105 mg and less than (<)150 mg of a type I IFN receptor (IFNAR1) inhibitor, wherein the IFNAR1 inhibitor is anifrolumab and wherein the unit dose is for subcutaneous injection to a subject once a week (QW).
2. The unit dose of claim 1, comprising equal to or less than ($\leq$)135 mg of the IFNAR1 inhibitor.
3. The unit dose of claim 1 or 2, comprising about 120 mg of the IFNAR1 inhibitor.
4. The unit dose of claim any of claims 1-3 for use in a method of treating or preventing disease in a subject, wherein the use comprises subcutaneous administration of the unit dose consists essentially of >105 mg and <150 mg of the IFNAR1 inhibitor to the subject, wherein the disease is a type I interferon (IFN)-mediated disease.
5. The unit dose for the use of claim 4, consisting essentially of $\leq$ 135 mg of the IFNAR1 inhibitor, wherein the disease is an autoimmune disease.
6. The unit dose for the use of claim 5, wherein the disease is lupus.
- 6.7. The unit dose for the use of claim 5, consisting essentially of about 120 mg of the IFNAR1 inhibitor, wherein the disease is SLE.
7. The unit dose for the use of any preceding claim 7, wherein the concentration of the IFNAR1 inhibitor/disease is about 150 mg/ml.
8. The unit dose of any preceding claim, wherein the volume of the unit dose is about 0.8 ml moderate to severe, active autoantibody-positive SLE.
9. The unit dose of any of the preceding claims use of claim 6, wherein the disease is lupus nephritis (LN).
10. The unit dose comprises a formulation of about 150 to 200 mg/ml of the IFNAR1 inhibitor, about 25 to 150 mM of lysine salt and an uncharged excipient use of claim 6, wherein the disease is cutaneous lupus erythematosus (CLE).
11. The unit dose for the use of claim 5, wherein the disease is myositis.
12. The unit dose for the use of claim 5, wherein the disease is scleroderma.
13. The unit dose of any of claims 1-3 for use in therapy.
14. Use of the unit dose of any of claims 1-3 in the manufacture of a medicament for treating or preventing disease in a subject, wherein the unit dose is to be administered subcutaneously to the subject, wherein the disease is a type I interferon (IFN)-mediated disease.

15. The use of claim 14, wherein the disease is an autoimmune disease.
16. The use of claim 15, wherein the disease is lupus.
17. The use of claim 16, wherein the disease is SLE.
18. The use of claim 17, wherein the disease is moderate to severe, active autoantibody-positive SLE.
19. The use of claim 16, wherein the disease is lupus nephritis (LN).
20. The use of claim 16, wherein the disease is cutaneous lupus erythematosus (CLE).
21. The use of claim 15, wherein the disease is myositis.
22. The use of claim 15, wherein the disease is scleroderma.

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- ~~10. The unit dose of claim 9, wherein the unit dose comprises a formulation of 25 mM histidine HCL, 130 mM trehalose, and 0.05% w/v polysorbate 80.~~
- ~~11. The unit dose of claim 9 or 10, wherein the formulation has a pH of about 5.9.~~
- ~~12. The unit dose of any of claims 1 to 11, wherein the IFNAR1 inhibitor is a human monoclonal antibody specific for IFNAR1, optionally a modified IgG1 class human monoclonal antibody.~~
- ~~13. The unit dose of claim 12, wherein the antibody comprises:~~
- ~~— (a) — a heavy chain variable region complementarity determining region 1 (HCDR1) comprising the amino acid sequence of SEQ ID NO: 3;~~
 - ~~— (b) — a heavy chain variable region complementarity determining region 2 (HCDR2) comprising the amino acid sequence of SEQ ID NO: 4;~~
 - ~~— (c) — a heavy chain variable region complementarity determining region 3 (HCDR3) comprising the amino acid sequence of SEQ ID NO: 5;~~
 - ~~— (d) — a light chain variable region complementarity determining region 1 (LCDR1) comprising the amino acid sequence SEQ ID NO: 6;~~
 - ~~— (e) — a light chain variable region complementarity determining region 2 (LCDR2) comprising the amino acid sequence SEQ ID NO: 7; and/or~~
 - ~~— (f) — a light chain variable region complementarity determining region 3 (LCDR3) comprising the amino acid sequence SEQ ID NO: 8.~~

- ~~14. The unit dose of claim 12 or 13, wherein the antibody comprises: (a) a human heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 1; and (b) a human light chain variable region comprising the amino acid sequence of SEQ ID NO: 2.~~
- ~~15. The unit dose of any of claims 11 to 14, wherein the antibody comprises an Fc region comprising an amino acid substitution of L234F, as numbered by the EU index as set forth in Kabat, and wherein said antibody exhibits reduced affinity for at least one Fc ligand compared to an unmodified antibody, optionally wherein the antibody comprises in the Fc region an amino acid substitution of L235E and/or P331S, as numbered by the EU index as set forth in Kabat.~~
- ~~16. The unit dose of any of claims 12 to 15, wherein the antibody comprises: (a) a human heavy chain comprising the amino acid sequence of SEQ ID NO: 11; and (b) a human light chain comprising the amino acid sequence of SEQ ID NO: 12.~~
- ~~17. The unit dose of any preceding claim, wherein the IFNAR1 inhibitor is anifrolumab or a functional variant thereof.~~
- ~~18. A method for treating a type I interferon (IFN)-mediated disease in a subject, the method comprising subcutaneously administering the unit dose of any of claims 1 to 17 to a subject having a type I interferon (IFN)-mediated disease.~~
- ~~19. A method of treating a type I IFN-mediated disease in a subject, the method comprising subcutaneously administering a dose of a IFNAR1 inhibitor to the subject, wherein the dose is more than (>)105 mg and less than (<)150 mg.~~
- ~~20. A method of treating a type I IFN-mediated disease in a subject, the method comprising subcutaneously administering a dose of a IFNAR1 inhibitor, wherein subcutaneously administering the dose every week provides a plasma concentration in the subject that is at least equivalent to the plasma concentration provided by intravenous administration of 300 mg of the IFNAR1 inhibitor every 4 weeks.~~
- ~~21. The method of claim 20, wherein subcutaneously administering the dose every week provides a plasma concentration in the subject that is more than the plasma concentration provided by intravenous administration of 300 mg of the IFNAR1 inhibitor every 4 weeks.~~
- ~~22. The method of any of claims 18 to 21, wherein the dose is <150 mg of the IFNAR1 inhibitor.~~
- ~~23. The method of any of claims 18 to 22, wherein the dose is >105 mg of the IFNAR1 inhibitor.~~
- ~~24. The method of any of claims 18 to 23, wherein the dose is subcutaneously administered in a single-administration step.~~

25. The method of any of claims 18 to 24, wherein the dose is equal to or less than ($\leq$) 135 mg of the IFNAR1 inhibitor.
26. The method of any of claims 18 to 25, wherein the dose is about 120 mg of the IFNAR1 inhibitor.
27. The method of any of claims 18 to 26, comprising subcutaneously administering the dose or unit dose at intervals of 6-8 days.
28. The method of any of claims 18 to 27, comprising subcutaneously administering the dose or unit dose once per week (QW).
29. The method of any of claims 18 to 28, wherein the dose or unit dose is 120 mg of the IFNAR1 inhibitor, and the method comprises subcutaneously administering the dose in a single administration step once per week (QW).
30. The method of any of claims 18 to 29, wherein the dose or unit dose is subcutaneously administered once per week for at least about 4, 8, 12, 16, 20, 24, 28, or 32 weeks.
31. The method of any of claims 18 to 30, wherein the dose or unit dose is subcutaneously administered once per week for at least about 8 weeks.
32. The method of any of claims 18 to 31, wherein the dose or unit dose has a volume of about 0.5 to about 1 ml.
33. The method of any of claims 18 to 32, wherein the dose or unit dose has a volume of about 0.8 ml.
34. The method of any of claims 18 to 33, comprising administering a corticosteroid to the patient, optionally wherein the corticosteroid is an oral corticosteroid.
35. The method of claim 34, comprising administering a first dose of the corticosteroid and subsequently administering a second dose of the corticosteroid, wherein the second dose of the corticosteroid is lower than the first dose of the corticosteroid.
36. The method of claim 35, wherein the second dose of the corticosteroid is about a 7.5 mg prednisone-equivalent dose or less; optionally wherein the second dose of the corticosteroid is a 5 mg prednisone-equivalent dose or less; optionally wherein the method comprises administering the second dose of the corticosteroid once per day.
37. The method of claim 35 or 36, wherein the first dose of the corticosteroid is about a 10 mg prednisone-equivalent dose.
38. The method of any one of claims 35 to 37, wherein the method comprises administering the second dose of the corticosteroid once per day.

39. The method of any one of claims 35 to 38, wherein the second dose of the corticosteroid is administered for at least 24 weeks, optionally for at least 28 weeks.
40. The method of any of claims 18 to 39, wherein administration of the dose or unit provides a plasma concentration of the IFNAR1 inhibitor in the subject of ≥ 10 $\mu\text{g/ml}$ of the functional variant thereof per ml of plasma (≥ 10 $\mu\text{g/ml}$).
41. The method of any of claims 18 to 40, wherein administration of the dose or unit dose provides a plasma concentration of the IFNAR1 inhibitor in the subject of about 10-100 $\mu\text{g/ml}$, optionally about 20-80 $\mu\text{g/ml}$, optionally about 30-70 $\mu\text{g/ml}$.
42. The method of any of claims 18 to 41, wherein administration of the dose or unit dose provides a trough concentration of the IFNAR1 inhibitor in the subject of ≥ 20 $\mu\text{g/ml}$; optionally ≥ 30 $\mu\text{g/ml}$; optionally ≥ 40 $\mu\text{g/ml}$.
43. The method of any of claims 18 to 42, wherein administration of the dose or unit dose provides a trough concentration of the IFNAR1 inhibitor in the subject of about 20-100 $\mu\text{g/ml}$, optionally about 30-80 $\mu\text{g/ml}$, optionally about 40-70 $\mu\text{g/ml}$.
44. The method of any of claims 18 to 43, wherein the subject is a type I interferon stimulated gene signature (IFNGS)-test high patient pre-administration with the dose or unit dose, optionally wherein the IFNGS is a 4-gene, 5-gene or 21-gene IFNGS.
45. The method of any of claims 18 to 44, comprising identifying the subject as a IFNGS-test high patient pre-treatment with the dose or unit dose.
46. The method of any of claims 18 to 45, wherein the dose or unit dose provides a therapeutic effect in the subject that is at least equivalent to a therapeutic effect provided by administration of an intravenous dose of 300 mg of the IFNAR1 inhibitor administered once every 4 weeks (Q4W).
47. The method of any of claims 18 to 46, wherein the dose or unit dose provides a trough concentration of the IFNAR1 inhibitor in the subject that is greater than a trough concentration of the IFNAR1 inhibitor provided by administration of an intravenous dose of 300 mg anifrolumab or the functional variant thereof once every 4 weeks (Q4W).
48. The method of any of claims 18 to 47, wherein the IFNAR1 inhibitor is comprised within a pharmaceutical composition.
49. The method of claim 48, wherein the pharmaceutical composition comprises 150 mg/mL of the IFNAR1 inhibitor, 50 mM lysine HCl, 130 mM trehalose dihydrate, 0.05% polysorbate 80 and 25 mM histidine/histidine HCl.

50. The method of any of claims 18 to 49, wherein the type I IFN-mediated disease is associated with an elevated IFNGS score compared to a healthy donor, wherein the IFNGS score is a 4-gene, 5-gene and/or 21-gene score.
51. The method of any of claims 18 to 50, wherein the type I IFN-mediated disease is an autoimmune disease.
52. The method of any of claims 18 to 51, wherein the type I IFN-mediated disease is lupus.
53. The method of claim 52, wherein the type I IFN-mediated disease is systemic lupus erythematosus (SLE), optionally wherein the SLE is moderate to severe, active autoantibody positive SLE.
54. The method of any of claim 52, wherein the type I IFN-mediated disease is lupus nephritis (LN).
55. The method of any of claim 52, wherein the type I IFN-mediated disease is cutaneous lupus erythematosus (CLE).
56. The method of any of claims 52 to 55, wherein administration of the dose or unit dose provides an improvement of the patient's BILAG-Based Composite Lupus Assessment (BICLA) response rate from baseline.
57. The method of any of claims 52 to 56, wherein administration of the dose or unit dose provides an improvement of the patient's Systemic Lupus Erythematosus Responder Index (SRI)4 score from baseline.
58. The method of any of claims 52 to 57, wherein the method reduces SLE disease activity in the subject.
59. The method of claim 58, wherein reducing SLE disease activity in the subject comprises:
- a) a BILAG-Based Composite Lupus Assessment (BICLA) response in the subject,
 - b) an SRI(4) response in the subject, and/or
 - c) reducing the subject's Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) score compared to the subject's CLASI score pre-treatment.
60. The method of any of claim 51, wherein the type I IFN-mediated disease is myositis.
61. The method of any of claim 51, wherein the type I IFN-mediated disease is scleroderma.
62. The method of any of claim 51, wherein the type I IFN-mediated disease is Sjogren's syndrome.
63. The method of any of claims 18 to 62, wherein the IFNAR1 inhibitor neutralises the elevated IFNGS in the subject.

64. The method of any of claims 18 to 63, wherein the IFNAR1 is a human monoclonal antibody specific for IFNAR1, optionally a modified IgG1 class human monoclonal antibody.
65. The method of claim 64, wherein the antibody comprises:
- (a) — a heavy chain variable region complementarity determining region 1 (HCDR1) comprising the amino acid sequence of SEQ ID NO: 3;
 - (b) — a heavy chain variable region complementarity determining region 2 (HCDR2) comprising the amino acid sequence of SEQ ID NO: 4;
 - (c) — a heavy chain variable region complementarity determining region 3 (HCDR3) comprising the amino acid sequence of SEQ ID NO: 5;
 - (d) — a light chain variable region complementarity determining region 1 (LCDR1) comprising the amino acid sequence SEQ ID NO: 6;
 - (e) — a light chain variable region complementarity determining region 2 (LCDR2) comprising the amino acid sequence SEQ ID NO: 7; and/or
 - (f) — a light chain variable region complementarity determining region 3 (LCDR3) comprising the amino acid sequence SEQ ID NO: 8.
66. The method of claim 64 or 65, wherein the antibody comprises: (a) a human heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 1; and (b) a human light chain variable region comprising the amino acid sequence of SEQ ID NO: 2.
67. The method of any of claims 64 to 65, wherein the antibody comprises an Fc region comprising an amino acid substitution of L234F, as numbered by the EU index as set forth in Kabat, and wherein said antibody exhibits reduced affinity for at least one Fc ligand compared to an unmodified antibody.
68. The method of any of claims 64 to 66, wherein the antibody comprises: (a) a human heavy chain comprising the amino acid sequence of SEQ ID NO: 11; and (b) a human light chain comprising the amino acid sequence of SEQ ID NO: 12.
69. The method of any of claims 18 to 68, wherein the IFNAR1 inhibitor is anifrolumab or a functional variant thereof.
70. The method of claim 19, wherein the type I IFN mediated disease is SLE, wherein the IFNAR1 inhibitor is anifrolumab or a functional variant thereof, wherein the dose is 120 mg, and wherein the method comprises subcutaneously administering the dose weekly.

- ~~71. The method of claim 19, wherein the type I IFN mediated disease is LN, wherein the IFNAR1 inhibitor is anifrolumab or a functional variant thereof, wherein the dose is 120 mg, and wherein the method comprises subcutaneously administering the dose weekly.~~
- ~~72. The method of claim 19, wherein the type I IFN mediated disease is CLE, wherein the IFNAR1 inhibitor is anifrolumab or a functional variant thereof, wherein the dose is 120 mg, and wherein the method comprises subcutaneously administering the dose weekly.~~
- ~~73. The method of claim 19, wherein the type I IFN mediated disease is myositis, wherein the IFNAR1 inhibitor is anifrolumab or a functional variant thereof, wherein the dose is 120 mg, and wherein the method comprises subcutaneously administering the dose weekly.~~
- ~~74. The method of claim 19, wherein the type I IFN mediated disease is scleroderma, wherein the IFNAR1 inhibitor is anifrolumab or a functional variant thereof, wherein the dose is 120 mg, and wherein the method comprises subcutaneously administering the dose weekly.~~
- ~~75. The method of claim 19, wherein the type I IFN mediated disease is Sjogren's syndrome, wherein the IFNAR1 inhibitor is anifrolumab or a functional variant thereof, wherein the dose is 120 mg, and wherein the method comprises subcutaneously administering the dose weekly.~~
- ~~76. A pharmaceutical composition for use in the method of treatment of any of claims 18 to 75, the method comprising subcutaneously administering the pharmaceutical composition to the subject, wherein the pharmaceutical composition comprises the unit dose of any of claims 1 to 17.~~
- ~~77. A pharmaceutical composition for use in a method of treating a type I IFN-mediated disease in a subject, the method comprising subcutaneously administering the pharmaceutical composition to a subject, wherein the pharmaceutical composition comprises a dose of anifrolumab or functional variant thereof, wherein the dose is more than (>)105 mg and less than (<)150 mg.~~
- ~~78. The pharmaceutical composition for the use of claim 76 or 77, wherein the dose is about 120 mg anifrolumab or the functional variant thereof.~~
- ~~79. An injection device comprising the unit dose of claims 1-17, or the pharmaceutical composition for the use of any of claims 76 to 78.~~
- ~~80. The injection device of claim 79, wherein the injection device is a pre-filled syringe (PFS).~~
- ~~81. The injection device of claim 79, wherein the injection device is an accessorized pre-filled syringe (AFPS).~~
- ~~82. The injection device of claim 79, wherein the injection device is an auto-injector.~~
- ~~83. A kit comprising i) the unit dose of any of claims 1 to 17, ii) the pharmaceutical composition of claim 77 or 78, or iii) the injection device of any of claims 79 to 82; and instructions for use, wherein the~~

instructions for use comprise instructions for subcutaneous administration of the unit dose or pharmaceutical composition to a subject.

84. ~~The kit of claim 83, wherein the instructions for use specify that the unit dose or pharmaceutical composition is for the use of any of the method of any of claims 18 to 75.~~

85. ~~The kit of claim 83 or 84, comprising packaging, wherein the packaging is adapted to hold the injection device and the instructions for use.~~

86. ~~The kit of any of claims 83 to 85, wherein the instructions for use are attached to the injection device.~~

87. ~~The kit of any of claims 83 to 86, wherein the instructions for use comprise instructions for administration of 120 mg anifrolumab or the functional variant.~~

88. ~~The kit of any of claims 83 to 87, wherein the instructions for use comprise instructions for subcutaneously administration of 120 mg anifrolumab or the functional variant every week.~~

89. ~~The kit of any of claims 83 to 87, wherein the instructions for use comprise instructions for use according to the method of any of claim 18 to 75.~~

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