

CLAIMS

- ~~1. A method of selecting a subject with SLE for treatment with a type I IFN receptor (IFNR) inhibitor, the method comprising selecting the subject for treatment if the subject's IL-10 plasma concentration is lower than a predetermined value, wherein the treatment reduces SLE disease activity in the subject.~~
- ~~2. The method of claim 1, comprising selecting the subject for treatment if the subject has an elevated IFNGS compared to a healthy subject.~~
- ~~3. The method of claim 2, wherein an elevated IFNGS comprises at least about four fold increase in mRNA of at least four of IFI27, IFI44, IFI44L, IFI6, and RSAD2 in a sample from the subject and/or subjects, relative to a sample from a healthy subject.~~
- ~~4. The method of claim 2, wherein an elevated IFNGS comprises at least about four fold increase in mRNA of at least four of IFI27, IFI44, IFI44L, IFI6, and RSAD2 in a sample from the subject and/or subjects, relative to pooled samples from healthy patients.~~
- ~~5. The method of claim 3 or 4, wherein an elevated IFNGS comprises at least about four fold increase in mRNA of at least four of IFI27, IFI44, IFI44L, IFI6, and RSAD2 in a sample compared to the mRNA of one or more control genes in the sample.~~
- ~~6. The method of claim 5, wherein the one or more control genes are chosen from ACTB, GAPDH, and 18S rRNA.~~
- ~~7. The method of any of claims 2 to 6, comprising detecting increased mRNA of IFI27, IFI44, IFI44L, and RSAD2 in the subject.~~
- ~~8. The method of any of claims 1 or 6, comprising selecting the subject for treatment if the subject is undergoing treatment comprising administration of OCS at a dose of 10 mg or more.~~
- ~~9. The method of any of claims 1 to 7, wherein the method is performed *in vitro*.~~
- ~~10. A method of selecting a subject with SLE for treatment with a type I IFN receptor (IFNR) inhibitor and an IL-10 inhibitor, the method comprising selecting the subject for treatment if the subject's IL-10 plasma concentration is higher than a predetermined value, wherein the treatment reduces SLE disease activity in the subject.~~
- 11.1. Use of anifrolumab in the manufacture of a medicament for A method of treating systemic lupus erythematosus (SLE) in a subject in need thereof, wherein the method comprising administering a therapeutically effective amount of an IFNR inhibitor the medicament is to be administered to the subject, wherein the subject has is identified as having an IL-10 plasma concentration lower than about 2 pg/ml at baseline a predetermined value, and wherein the medicament treatment reduces SLE disease activity in the subject.

- ~~12.2.~~ The ~~use method~~ of claim ~~110 or 11~~, wherein the subject ~~has is identified as having an~~ elevated type I IFN gene signature (IFNGS) at baseline compared to a healthy subject.
- ~~13.3.~~ The ~~use method~~ of claim ~~212~~, wherein an elevated IFNGS comprises at least ~~about~~ four-fold increase in mRNA of at least four of IFI27, IFI44, IFI44L, IFI6, and RSAD2 in a sample from the subject and/or subjects, relative to a sample from a healthy subject.
- ~~14.4.~~ The ~~use method~~ of claim ~~212~~, wherein an elevated IFNGS comprises at least ~~about~~ four-fold increase in mRNA of at least four of IFI27, IFI44, IFI44L, IFI6, and RSAD2 in a sample from the subject and/or subjects, relative to pooled samples from healthy patients.
- ~~15.5.~~ The ~~use method~~ of claim ~~213 or 14~~, wherein an elevated IFNGS comprises at least four-fold increase in the mRNA of at least four of IFI27, IFI44, IFI44L, IFI6, and RSAD2 in a sample compared ~~is increased relative to the mRNA of one or more control genes present in the sample.~~
- ~~16.6.~~ The ~~use method~~ of claim ~~515~~, wherein the one or more control genes are chosen from ACTB, GAPDH, and 18S rRNA.
- ~~17.~~ The method of any of claims 11 to 16, comprising detecting increased mRNA of IFI27, IFI44, IFI44L, and RSAD2 in the subject.
- ~~18.~~ The method of claim 11 to 17, wherein, the subject is undergoing treatment comprising administration of OCS at a dose of 10 mg or more pre-treatment with the IFNAR1 inhibitor.
- ~~19.~~ A method of treating SLE in a subject in need thereof, the method comprising administering a therapeutically effective amount of an IFNR inhibitor and an IL-10 inhibitor, wherein the subject is identified as having an IL-10 plasma concentration higher than a predetermined value, wherein the treatment SLE disease activity.
- ~~20.~~ A method of selecting a subject with SLE for treatment with an anti-BAFF monoclonal antibody, the method comprising selecting the subject for treatment if the subject's IL-10 plasma concentration is higher than a predetermined value, wherein the treatment reduces SLE disease activity in the subject.
- ~~21.~~ The method of claim 20, wherein the anti-BAFF antibody is belimumab or a functional variant thereof.
- ~~22.~~ A method of treating SLE in a subject in need thereof, the method comprising administering a therapeutically effective amount of an anti-BAFF monoclonal antibody and an anti-CD20 antibody, wherein the subject is identified as having an IL-10 plasma concentration higher than a predetermined value, wherein the treatment reduces SLE disease activity.
- ~~23.~~ The method of claim 22, wherein the anti-CD20 antibody is rituximab and the anti-BAFF antibody is belimumab.

24. The method of any preceding claim, comprising determining the IL-10 concentration in a sample from the patient, optionally wherein the sample is isolated from the subject.
- 25.7. ~~The use method of any preceding claim 24, wherein the method comprises measuring the IL-10 concentration in the a plasma sample from the patient subject is measured.~~
- 26.8. ~~The use method of claim 725, wherein the IL-10 concentration is measured by immunoassay, optionally wherein the immunoassay is a Luminex or Simoa immunoassay.~~
27. The method of claim 26, wherein the immunoassay is a Luminex or Simoa immunoassay.
28. The method of any of claims 24 to 27, wherein the sample is a blood, serum or plasma sample.
29. The method of any preceding claim, wherein the predetermined value is less than 1.5 pg/ml, about 1.5 to 2.5 pg/ml, about 25 to 2.8 pg/ml or about 1 to about 3.5 pg/ml.
30. The method of any preceding claim, wherein the predetermined value is about 1.5 to about 2.5 pg/ml.
31. The method of claim 27, wherein the predetermined value is about 1.7 to 2.3 pg/ml.
32. The method of any of claims 1 to 29, wherein the predetermined value is about 1.0, about 1.1, about 1.2, about 1.3, about 1.4, about 1.5, about 1.6, about 1.7, about 1.8, about 1.9, about 2.0, about 2.1, about 2.2, about 2.3, about 2.4, about 2.5, about 2.6, about 2.7, about 2.8, about 2.9, about 3.0, about 3.1, about 3.2, about 3.3, about 3.4, about 3.5, about 1, about 2 or about 3.
33. ~~The method of any of claims 1 to 29, The method of any of claims 1 to 8, wherein the predetermined value is 1.0, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2.0, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3.0, 3.1, 3.2, 3.3, 3.4, 3.5, 1, 2 or 3 pg/ml.~~
34. The method of claim 29, wherein the predetermined value is about 2 pg/ml.
35. The method of claim 29, wherein the predetermined value is 2 pg/ml.
36. ~~The method of any of claims 1 to 26, wherein the predetermined value is determined by: a) determining or measuring the IL-10 plasma concentrations of subjects in a sample population of subjects with SLE; b) determining or measuring the median IL-10 concentration in the population of subjects with SLE, wherein the predetermined value is the median determined in b).~~
37. The method of any preceding claim, wherein the subject is undergoing treatment comprising administration of OCS at a dose of 10 mg or more pre-treatment with the IFN γ inhibitor.
38. The method of any preceding claim, 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,

- ~~c. reducing the subject's Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) score compared to the subject's CLASI score pre-treatment,~~
 - ~~d. reducing the subject's tender and swollen joint count compared to the subject's tender and swollen joint count pre-treatment,~~
 - ~~e. the subject having a maximum of 1 BILAG-2004 B score following treatment,~~
 - ~~f. the subject having a BILAG-2004 score of C or better following treatment,~~
 - ~~g. the subject having an improvement in at least one patient reported outcome (PRO) compared to pre-treatment, and/or~~
 - ~~h. reducing the subject's SLE flare rate compared to the subject's flare rate pre-treatment.~~
- ~~39. The method of any preceding claim, comprising measuring the subject's BILAG score before and after administration of the IFNAR1 inhibitor.~~
- ~~40. The method of any preceding claim, wherein the BICLA response is sustained in the subject for at least 52 weeks.~~
- ~~41. The method of any preceding claim, comprising measuring PROs in the subject before and after administration of the IFNR inhibitor.~~
- ~~42. The method of claim 41, wherein the PRO's comprise the subject's Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-F), Short Form 36 Health Survey version 2 (SF-36-v2), mental component summary (MCS), and/or SF-36, physical component summary (PCS) score.~~
- ~~43. The method of any preceding claim, wherein the BICLA response comprises reduction of the subject's BILAG-2004 A and B domain scores to B/C/D and C/D, respectively.~~
- ~~44. The method of any preceding claim, wherein reducing the subject's CLASI score compared to the subject's CLASI score pre-treatment comprises a reduction in the subject's CLASI-A score compared to the subject's CLASI-A score pre-treatment.~~
- ~~45. The method of any preceding claim, wherein the reducing the SLE disease activity in the subject comprises reducing the anti-dsDNA levels in the subject.~~
- ~~46. The method of any preceding claim wherein the reducing SLE disease activity in the subject comprises a BILAG-Based Composite Lupus Assessment (BICLA) response, and wherein the method comprises reducing the OCS dose administered to the subject compared to the OCS dose administered to the subject pre-treatment~~
- ~~47. The method of claim 46, wherein the OCS comprises prednisone, prednisolone and/or methylprednisolone.~~
- ~~48. The method of any preceding claim, wherein the reducing SLE disease activity in the subject comprises a BILAG-Based Composite Lupus Assessment (BICLA) response by at least week 4 of treatment.~~

- ~~49. The method of any preceding claim, wherein the reducing SLE disease activity comprises a BILAG-Based Composite Lupus Assessment (BICLA) response by at least week 8 of treatment.~~
- ~~50. The method of any preceding claim, wherein the reducing SLE disease activity in the subject comprises at least a 50% improvement in the tender joint count and swollen joint count in the subject compared to the tender joint and swollen count in the subject pre treatment value.~~
- ~~51. The method of any preceding claim, wherein the reduction in the subject's CLASI score is achieved by at least week 8 of treatment.~~
- ~~52. The method of any preceding claim, wherein the reduction in the subject's CLASI score is achieved following 12 weeks of treatment.~~
- ~~53. The method of any preceding claim, wherein reducing SLE disease activity in the subject comprises at least 50% reduction in the subject's CLASI score compared to the subject's CLASI score pre treatment.~~
- ~~54. The method of claim 53, wherein reducing SLE disease activity in the subject comprises reduction of the subject's CLASI-A score following 12 weeks of treatment.~~
- ~~55. The method of claim 53 or 54, wherein the subject has a CLASI-A score of ≥ 10 pretreatment.~~
- ~~56. The method of any preceding claim, wherein reducing SLE disease activity in the subject comprises the subject's BILAG-2004 score being C or better after 24 weeks of treatment.~~
- ~~57. The method of any preceding claim, wherein reducing SLE disease activity in the subject comprises the subject having a maximum of 1 BILAG-2004 B score after 24 weeks of treatment.~~
- ~~58. The method of any preceding claim, wherein reducing SLE disease activity in the subject comprises a reduction in the subject's BILAG-based annualized flare rate compared to the subject's BILAG-based annualized flare rate pre treatment.~~
- ~~59. The method of any preceding claim, wherein reducing SLE disease activity in the subject comprises preventing flares in the subject.~~
- ~~60. The method of any preceding claim, wherein a flare is defined as ≥ 1 new BILAG-2004 A or ≥ 2 new (worsening) BILAG-2004 B domain scores compared to the subject's scores one month previously.~~
- ~~61. The method of any preceding claim, wherein reducing SLE disease activity in the subject comprises a reduced flare rate in the subject compared to the flare rate pre treatment, wherein the method comprises reducing OCS dose administration to the subject compared to the OCS dose administered to the subject pre treatment.~~
- ~~62. The method of any preceding claim, comprising selecting the subject for treatment, wherein the subject is selected for having active SLE.~~

- ~~63. The method of any preceding claim, comprising selecting the subject for treatment, wherein the subject is selected for having moderate to severe SLE.~~
- ~~64. The method of any preceding claim, wherein the subject is selected for having SLE that is unresponsive to OCS treatment.~~
- ~~65. The method of any preceding claim, wherein the subject is an adult.~~
- ~~66. The method of any preceding claim, wherein the type I IFN receptor inhibitor is administered intravenously.~~
- ~~67. The method of any preceding claim wherein the type I IFN receptor inhibitor is an anti type I interferon receptor antibody or antigen binding fragment thereof that specifically binds IFNAR1.~~
- ~~68. The method of claim 67, wherein the IFNR inhibitor is a monoclonal antibody.~~
- ~~69. The method of claim 69, wherein the IFNR inhibitor 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;~~
 - ~~a heavy chain variable region complementarity determining region 3 (HCDR3) comprising the amino acid sequence of SEQ ID NO: 5;~~
 - ~~c) a light chain variable region complementarity determining region 1 (LCDR1) comprising the amino acid sequence SEQ ID NO: 6;~~
 - ~~d) a light chain variable region complementarity determining region 2 (LCDR2) comprising the amino acid sequence SEQ ID NO: 7; and/or~~
 - ~~e) a light chain variable region complementarity determining region 3 (LCDR3) comprising the amino acid sequence SEQ ID NO: 8.~~
- ~~70. The method of claim 68, wherein the IFNR inhibitor 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.~~
- ~~71. The method of any of claims 68 to 70, wherein the IFNR inhibitor comprise an Fc region comprising an amino acid substitution of L234F, as numbered by the EU index as set forth in Kabat, and wherein the 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 L234F, L235E and/or P331S, as numbered by the EU index as set forth in Kabat.~~

- ~~72. The method of any of claims 68 to 71, wherein the IFNR inhibitor comprises (a) a human 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.~~
- ~~73. The method of claim 68, wherein the IFNR inhibitor is anifrolumab or a functional variant thereof.~~
- ~~74. The method of claim 73, wherein the treatment comprises administering anifrolumab or a functional variant thereof.~~
- ~~75.9. The use method of any preceding claim 73, wherein the medicament treatment comprises administering 300 mg anifrolumab or the functional variant thereof.~~
- ~~76.10. The use method of claim 968 or 67, wherein the medicament anifrolumab or functional variant thereof is to be administered to the subject as an intravenous (IV) infusion.~~
- ~~77.11. The use method according to any of claims 1067 to 70, wherein the medicament anifrolumab or functional variant thereof is to be administered the subject every 4 four weeks.~~
- ~~78.12. The use method of any one of claims 1 to 8 73, wherein the medicament treatment comprises administering about 120 mg anifrolumab or the functional variant thereof.~~
- ~~79.13. The use method of claim 1278, wherein the medicament anifrolumab or functional variant thereof is to be administered subcutaneously.~~
- ~~80.14. The use method according to any of claims 1378 to 79, wherein the medicament anifrolumab or functional variant thereof is to be administered to the subject every week.~~
- ~~81. The method according to any of claim 73 to 80, wherein anifrolumab or the functional variant thereof is provided in a solution at a concentration of 150 mg/mL.~~
- ~~82. A pharmaceutical composition for use in a method of treating SLE in a subject in need thereof, the method of treatment comprises administering a therapeutically effective amount of an IFNR inhibitor, wherein the subject is identified as having an IL-10 plasma concentration lower than a predetermined value, wherein the treatment reduces SLE disease activity.~~
- ~~83. The pharmaceutical composition for the use of claim 73, wherein the IFNR inhibitor is anifrolumab or a functional variant thereof.~~
- ~~84. The pharmaceutical composition for the use of claim 83, wherein the pharmaceutical composition comprises anifrolumab or the functional variant thereof at a concentration of 150 mg/mL.~~
- ~~85. A kit comprising the pharmaceutical composition of any of claims 82 to 83 and instructions for use, wherein the instructions for use specify any of the methods of claims 1 to 81.~~
- ~~86. The kit of claim 85, comprising an IL-10 inhibitor.~~

15. The use of any of any preceding claim, wherein the subject has moderate to severe SLE.