

CLAIMS

1. A pharmaceutical composition for use in a method of treating or reducing the risk for development of a cardiometabolic disease in a patient in need thereof, wherein the pharmaceutical composition comprises ~~the method comprising administering to the patient a~~ therapeutically effective amount of an inhibitor of type I IFN signalling, wherein the pharmaceutical composition is to be administered to the patient, and wherein the patient has a type I IFN mediated disease.
2. The pharmaceutical composition for use of claim 1, wherein ~~The method of any preceding claim, wherein,~~ pre-treatment with the pharmaceutical composition ~~inhibitor of type I IFN signalling,~~ the patient has high levels of expression of the one or more cardiometabolic disease markers compared to a healthy subject, and wherein treatment reduces expression of the one or more cardiometabolic disease markers in the patient from baseline, wherein the one or more cardiometabolic disease markers comprise GlycA; neutrophil extracellular trap (NET); or TNF- α and/or IL-10. -
3. ~~The method of claim 2, wherein the one or more cardiometabolic disease markers comprise GlycA.~~
4. ~~The method of claim 2 or 3, wherein the one or more cardiometabolic disease markers comprise neutrophil extracellular trap (NET).~~
5. ~~The method of any of claims 2 to 4, wherein the one or more cardiometabolic disease markers comprise TNF- α and/or IL-10.~~ 6. ~~The method of any preceding claim, wherein, pre-treatment with the inhibitor of type I IFN signalling, the patient has low levels of expression of the one or more cardiometabolic disease markers compared to a healthy subject, and wherein treatment increases expression of the one or more cardiometabolic disease markers in the patient from baseline.~~
7. ~~The method of claim 6, wherein the one or more cardiometabolic disease markers comprise cholesterol efflux capacity (CEC).~~
3. 8. The pharmaceutical composition for use of claim 1 or 2, The method of any preceding claim, wherein pre-treatment, the patient is identified as having a risk of development of a cardiometabolic disease.
- 4.9. The pharmaceutical composition for use of ~~The method of claim 38, wherein~~ comprising:
 - a) determining in a sample from the patient the amount of one or more markers is to be determined in a sample from the patient; and

- b) ~~identifying the patient is to be identified~~ as having a risk for development of a cardiometabolic disease when the amount of marker is elevated in the patient compared to the amount of the marker in a sample from a healthy subject,

wherein the marker is selected from the group consisting of GlycA, TNF- α , IL-10 and combinations thereof.

~~10. The method of claim 9, wherein the sample from the patient comprises blood, plasma, serum, or tissue.~~

~~11. The method of claim 9 or 10, wherein GlycA in the sample from the patient is measured by nuclear magnetic resonance (NMR).~~

~~5.12.~~ The pharmaceutical composition for use of any preceding claim~~The method of any preceding claim~~, wherein pre-treatment with the inhibitor of type I IFN signalling the patient has elevated serum protein levels of IFN- α compared to a healthy subject, and wherein the inhibitor of type I IFN signalling decreases the serum protein levels of IFN- α in the patient from baseline.

~~6.13.~~ The pharmaceutical composition for use of ~~The method of any preceding claim,~~ wherein the inhibitor of type I IFN signalling is a type I IFN receptor inhibitor (IFNAR1), optionally wherein the -

~~14. The method of claim 13, wherein the IFNAR1 inhibitor is a human monoclonal antibody specific for IFNAR1, optionally a modified IgG1 class human monoclonal antibody.~~

~~7.15.~~ The pharmaceutical composition for use of ~~The method of claim 614,~~ 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
- f) a light chain variable region complementarity determining region 3 (LCDR3) comprising the amino acid sequence SEQ ID NO: 8.

- ~~8.16.~~ The pharmaceutical composition for use ~~The method of claim 6 or claim 7~~ claim 14 or 15, wherein the antibody comprises: (a) a human heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 1; (b) a human light chain variable region comprising the amino acid sequence of SEQ ID NO: 2; (c) a human light chain constant region comprising the amino acid sequence of SEQ ID NO: 9; and (d) a human heavy chain constant region comprising the amino acid sequence of SEQ ID NO: 10.
- ~~9.17.~~ The pharmaceutical composition for use of ~~The method of any of claims 14 to 16~~ any of claims 7 or claim 8, wherein the antibody comprises in the Fc region 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.
- ~~10.18.~~ The pharmaceutical composition for use of any of ~~The method of any of claims 14-7 to 17~~ 9, 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.
- ~~11.19.~~ The pharmaceutical composition for use of ~~The method of any~~ preceding claim, wherein the inhibitor of type I IFN signalling is anifrolumab or a functional variant thereof.
- ~~12.20.~~ The pharmaceutical composition for use of ~~The method of claim 11~~ 19, comprising administering intravenously an intravenous dose of anifrolumab or the functional variant thereof is to be administered intravenously to the subject, optionally wherein the -
- ~~21.~~ The method of claim 20, wherein the intravenous dose is ≥ 300 mg and ≤ 1000 mg anifrolumab or the functional variant thereof, optionally wherein the -
- ~~22.~~ The method of claim 20 or 21, wherein the intravenous dose is ≤ 1000 mg.
- ~~23.~~ The method of claim 21, wherein the intravenous dose is about 300 mg or about 1000 mg.
- ~~13.24.~~ The pharmaceutical composition for use of ~~The method of any of claims 20 to 23~~ claim 12, wherein the intravenous dose is to be administered every four weeks (Q4W).
- ~~14.25.~~ The pharmaceutical composition for use of claim 13, wherein ~~The method of any preceding claim, wherein the patient has high interferon gene signature expression compared to a healthy subject.~~
- ~~26.~~ The method of claim 25, wherein the type I interferon gene signature comprises elevated expression of the genes Interferon Alpha Inducible Protein 27 (IFI27), Interferon Induced Protein 44 (IFI44) interferon induced protein 44 like (IFI44L), and Radical S-Adenosyl Methionine Domain Containing 2 (RSAD2) compared to a healthy subject.
- ~~27.~~ The method of claim 25 or 26, wherein the high interferon gene signature expression is determined by an increased expression of IFI27, IFI44, IFI44L, and RSAD2 relative to expression of one or more control genes.

- ~~28. The method of any preceding claim, wherein the cardiometabolic disease is a cardiovascular disease, optionally wherein the cardiovascular disease comprises myocarditis, arrhythmia, valvular dysfunction, vasculitis, aortitis, atherosclerosis and/or coronary vasculitis, optionally wherein.~~
- ~~29. The method of any preceding claim, wherein the cardiometabolic disease is premature atherosclerosis, optionally.~~
- ~~30. The method of claim 29, wherein the premature atherosclerosis is sub-clinical.~~
- ~~15.31. The pharmaceutical composition for use method of any preceding claim, wherein the type I IFN mediated disease is systemic lupus erythematosus (SLE), optionally wherein.~~
- ~~32. The method of claim 31, the type I IFN mediated disease is moderate to severe SLE.~~
- ~~33. A pharmaceutical composition for use in any of the methods of claims 1-32, comprising the inhibitor of type I IFN signalling.~~
- ~~34. An injection device comprising the pharmaceutical composition of claim 33.~~
- ~~35. The injection device of claim 34, wherein the injection device is a pre-filled syringe (PFS).~~
- ~~36. The injection device of claim 35, wherein the injection device is an accessorized pre-filled syringe (AFPS).~~
- ~~37. The injection device of claim 35, wherein the injection device is an auto-injector.~~
- ~~38. A kit comprising the injection device of any of claims 34 to 37, and instructions for use.~~
- ~~39. The kit of claim 38, wherein the instructions for use comprise instructions for subcutaneous administration of the pharmaceutical composition or unit dose to the patient.~~
- ~~40. The kit of claim 35 or 39, wherein the instructions for use specify that the injection device and/or pharmaceutical composition are for use in the treatment of SLE.~~
- ~~41. The kit of any of claims 35-40, wherein the instructions for use specify that the injection device and/or pharmaceutical composition are for treating a cardiometabolic disease.~~
- ~~42. The kit of any of claims 35 to 41, comprising packaging, wherein the packaging is adapted to hold the injection device and the instructions for use.~~
- ~~43. The kit of any of claims 35 to 42, wherein the instructions for use are attached to the injection device.~~