

CLAIMS

1. Use of an IL-2 agent in the manufacture of a medicament for treating an autoimmune disease in a human subject, wherein the IL-2 agent is to be administered at a dose of 0.5 µg/kg to 300 µg/kg, wherein the IL-2 agent is an IL-2 variant or an IL-2 fusion protein comprising the IL-2 variant, and wherein the IL-2 variant comprises:

- (i) the amino acid substitution H16L or H16N, and/or the amino acid substitution I92S; and
- (ii) the amino acid substitutions V69A, Q74P, and C125S, corresponding to human IL-2 (SEQ ID NO: 1031).

2. The use of claim 1, wherein the IL-2 agent is to be administered at a dose of 0.5 µg/kg to 100 µg/kg, 1 µg/kg to 50 µg/kg, 2 µg/kg to 40 µg/kg, 3 µg/kg to 30 µg/kg, 4 µg/kg to 25 µg/kg, 5 µg/kg to 20 µg/kg, 10 µg/kg to 15 µg/kg, 1 µg/kg to 40 µg/kg, 1 µg/kg to 30 µg/kg, 1 µg/kg to 20 µg/kg, 1 µg/kg to 10 µg/kg, 1 µg/kg to 5 µg/kg, 5 µg/kg to 50 µg/kg, 10 µg/kg to 50 µg/kg, 20 µg/kg to 50 µg/kg, 30 µg/kg to 50 µg/kg, 40 µg/kg to 50 µg/kg, 0.5 µg/kg to 2 µg/kg, 3 µg/kg to 5 µg/kg, 6 µg/kg to 10 µg/kg, 12 µg/kg to 20 µg/kg, or 25 µg/kg to 40 µg/kg.

3. The use of claim 1 or 2, wherein the IL-2 agent is to be administered at a dose of 1 µg/kg, 4 µg/kg, 8 µg/kg, 16 µg/kg, or 32 µg/kg.

4. The use of any of claims 1 to 3, wherein the IL-2 agent is to be administered once a week, once every two weeks, or once every four weeks.

5. The use of any of claims 1 to 4, wherein the IL-2 agent is to be administered subcutaneously.

6. The use of any of claims 1 to 5, wherein the autoimmune disorder is systemic lupus erythematosus (SLE), autoimmune hepatitis (AIH), immune-mediated focal segmental glomerulosclerosis (FSGS), or alopecia areata (AA).

7. The use of any of claims 1 to 6, wherein the IL-2 variant further comprises the amino acid substitution T3A.

8. The use of any of claims 1 to 7, wherein the IL-2 variant comprises the amino acid sequence of any of SEQ ID NOs: 4, 5, 11, 1000, 1001, or 1002, an amino acid sequence that is at least 95% identical thereto.

9. The use of any of claims 1 to 8, wherein the IL-2 agent comprises an IL-2 fusion protein comprising the IL-2 variant.
10. The use of claim 9, wherein the IL-2 fusion protein further comprises an Fc region.
- 5 11. The use of claim 10, wherein the Fc region comprises an Fc region of IgG1 allotype m3 comprising an N297G substitution according to EU numbering.
12. The use of claim 10 or 11, wherein the Fc region comprises the amino acid sequence of SEQ ID NO: 1003, or an amino acid sequence that is at least 95% identical thereto.
- 10 13. The use of any of claims 10 to 12, wherein the Fc region is fused to the C-terminus of the IL-2 variant.
- 15 14. The use of any of claims 10 to 13, wherein the IL-2 fusion protein further comprises a linker.
15. The use of claim 14, wherein the linker comprises (G4S)₄ (SEQ ID NO: 48).
16. The use of any of claims 10 to 15, wherein the fusion protein comprises an amino acid sequence of any of SEQ ID NOs: 1004, 1005, 1006, 1007, 1008, or 1009, an amino acid sequence that is at least 95% identical thereto.
- 20 17. The use of any of claims 10 to 16, wherein the fusion protein forms a dimer.