

## CLAIMS:

1. A method of treating or preventing chronic Graft versus Host Disease (cGvHD) in a human subject in need thereof, the method comprising administering to the subject a composition comprising culture expanded mesenchymal lineage precursor or stem cells (MLPSCs).
2. The method of claim 1, wherein the MLPSCs have been cryopreserved and thawed.
3. The method of claim 1 or claim 2, wherein the MLPSCs are culture expanded from an intermediate cryopreserved MLPSCs population.
4. The method according to any one of claims 1 to 3, wherein the MLPSCs are culture expanded for at least about 5 passages.
5. The method of any one of claims 1 to 4, wherein the MLPSCs express at least 13 pg TNFR1 per million MLPSCs.
6. The method of any one of claims 1 to 4, wherein the MLPSCs express about 13 pg to about 44 pg TNFR1 per million MLPSCs.
7. The method of any one of claims 1 to 6, wherein said culture expansion comprises at least 20 population doublings.
8. The method of any one of claims 1 to 6, wherein said culture expansion comprises at least 30 population doublings.
9. The method according to any one of claims 1 to 8, wherein the subject is refractory to steroid immunosuppressant and/or a biologic therapy.

10. The method according to any one of claims 1 to 9, wherein the subject has at least a partial response after 28 days of treatment.
11. The method according to any one of claims 1 to 9, wherein the subject has at least a partial response at least 28 to 90 days after treatment.
12. The method of claim 10 or 11 wherein a partial response is characterized by one or more or all of:
  - Reduction in Skin % BSA score of at least one point;
  - Reduction in mouth score of at least one point;
  - Reduction in eye score of at least one point;
  - Reduction in skin features score of at least one point;
  - Reduction in gastrointestinal tract score of at least one point;
  - Reduction in liver score of at least one point;
  - Reduction in lung symptom score of at least one point;
  - Reduction in lung FEV1 score of at least one point;
  - Reduction in joints and fascia score of at least one point;
  - Reduction in genital tract score of at least one point.
13. The method of claim 10 or 11 wherein a partial response is characterized by one or more or all of:
  - Reduction in Skin % BSA score of at least one point;
  - Reduction in mouth score of at least one point;
  - Reduction in eye score of at least one point.
14. The method according to any one of claims 1 to 13, wherein the MLPSCs are administered intravenously.
15. The method according to any one of claims 1 to 14, wherein the MLPSCs are mesenchymal stem cells (MSCs).

16. The method according to any one of claims 1 to 15, wherein the MLPSCs are allogeneic.
17. The method according to any one of claims 1 to 16 which comprises administering between  $10 \times 10^6$  and  $2 \times 10^8$  cells per dose.
18. The method according to any one of claims 1 to 16 which comprises administering between  $20 \times 10^6$  and  $1 \times 10^7$  cells per dose.
19. The method according to claim 17 or 18, wherein the subject receives at least two doses.
20. The method according to claim 17 or 18, wherein the subject receives at least 2, 3, 4, 5, 6, 7, 8, 9 or 10 doses.
21. The method of claim 19 or 20, wherein the first two doses are administered weekly for two weeks.
22. The method of claim 19 or 20, wherein the first two doses are administered weekly every two weeks.
23. The method of claim 22, wherein third and subsequent doses are administered monthly.
24. The method according to any one of claims 1 to 23, wherein the composition further comprises Plasma-Lyte A, dimethyl sulfoxide (DMSO), human serum albumin (HSA).
25. The method according to any one of claims 1 to 23, wherein the composition further comprises Plasma-Lyte A (70%), DMSO (10%), HSA (25%) solution, the HSA solution comprising 5% HSA and 15% buffer.

26. The method according to any one of claims 1 to 25, wherein the composition comprises greater than  $6.68 \times 10^6$  viable cells/mL.

**CLAIMS**

1. Use of a composition comprising culture expanded mesenchymal lineage precursor or stem cells (MLPSCs) in the preparation of a medicament for treatment of chronic Graft versus Host Disease (cGvHD) in a human subject, in which the composition is to be intravenously administered at a dose of  $1 \times 10^6$  MLPSCs/kg to  $3 \times 10^6$  MLPSCs/kg, in which the MLPSCs have been cryopreserved and thawed, and in which the subject has at least a partial response 28 days to 90 days after treatment.
2. Use according to Claim 1, in which the MLPSCs are culture expanded from an intermediate cryopreserved MLPSC population.
3. Use according to Claim 1 or 2, in which the MLPSCs are culture expanded for at least 5 passages.
4. Use according to Claim 1, 2 or 3, in which the MLPSCs express at least 13 pg TNFR1 per million MLPSCs, preferably between 13 pg to 44 pg TNFR1 per million MLPSCs.
5. Use according to any preceding claim, in which the subject is refractory to steroid immunosuppressant and/or a biologic therapy.
6. Use according to any preceding claim, in which a partial response is characterized by one or more or all of:
  - reduction in Skin % BSA score of at least one point;
  - reduction in mouth score of at least one point;
  - reduction in eye score of at least one point;
  - reduction in skin features score of at least one point;
  - reduction in gastrointestinal tract score of at least one point;
  - reduction in liver score of at least one point;
  - reduction in lung symptom score of at least one point;
  - reduction in lung FEV1 score of at least one point;
  - reduction in joints and fascia score of at least one point; and

reduction in genital tract score of at least one point.

7. Use according to Claim 6 , in which a partial response is characterized by one or more or all of:

reduction in Skin % BSA score of at least one point;

5 reduction in mouth score of at least one point; and

reduction in eye score of at least one point.

8. Use according to any preceding claim, in which the MLPSCs are mesenchymal stem cells (MSCs).

9. Use according to any preceding claim, in which the composition further comprises

10 Plasma-Lyte A, dimethyl sulfoxide (DMSO), human serum albumin (HSA), preferably Plasma-Lyte A (70%), DMSO (10%), HSA (25%) solution, the HSA solution comprising 5% HSA and 15% buffer.

10. Use according to any preceding claim, in which the composition comprises greater than  $6.68 \times 10^6$  viable cells/mL.