WHAT IS CLAIMED IS:

1. A method of reducing pain or reducing opioid use or increasing EQ-5D score, the method comprising administering to the subject a composition comprising mesenchymal lineage precursor or stem cells (MLPSCs), wherein the subject is using an opioid.

2. The method of claim 1, wherein the composition comprises hyaluronic acid (HA).

3. The method of claim 1 or claim 2, wherein the subject is using an opioid for pain.

4. An opioid sparing composition comprising mesenchymal lineage precursor or stem cells (MLPSCs).

5. The composition of claim 4, further comprising hyaluronic acid (HA), preferably 1% HA.

6. The composition of claim 4 or claim 5, wherein the opioid sparing composition is administered to a subject using an opioid, preferably, wherein the subject is using the opioid for pain.

7. The method according to any one of claims 1 to 3 or the composition of claim 6, wherein of the pain is chronic pain.

8. The method according to any one of claims 1 to 3 or the composition according to any one of claims 4 to 7, wherein pain is lower back pain, preferably wherein the lower back pain is associated with a degenerated disc.

9. The method or composition of claim 7, wherein the lower back pain is associated with an intervertebral disc, preferably wherein the disc has a disc height that is not substantially reduced compared to that of an adjacent healthy disc in the subject.

10. The method or composition of claim 7, wherein the lower back pain is non-radicular in origin and/or is associated with one or more of:
    - an intervertebral disc herniation up to a 3mm protrusion.
    - nerve ingrowth into an intervertebral disc.
    - inflammation in an intervertebral disc.

11. The method or composition claim 10, wherein the nerve ingrowth or inflammation is in the intervertebral disc space, or the nucleus pulposus, or the annulus fibrosis of the intervertebral disc.

12. The method according to any one of claims 1 to 3 or 6 to 11 or the composition according to any one of claims 5 to 11, wherein opioid use is reduced 1 month, preferably 3 months after administration of the composition.

13. The method according to any one of claims 1 to 3 or 6 to 11 or the composition according to any one of claims 5 to 11, wherein opioid use is reduced 6 months, preferably 12 months, more preferably 18 months, even more preferably 24 months after administration of the composition.

14. The method according to any one of claims 1 to 3 or 7 to 11 or the composition according to any one of claims 5 to 11, wherein opioid use is reduced for at least 12 months, preferably at least 24 months after administration of the composition.

15. The method according to any one of claims 1 to 3 or 6 to 14 or the composition according to any one of claims 5 to 14, wherein opioid use is reduced relative to the subjects average baseline morphine equivalent dose prior to administering the composition.

16. The method according to any one of claims 1 to 3 or 6 to 15, wherein the subject has been using an opioid for at least 1 month, preferably at least 3 months, more preferably at least 6 months prior to administering the composition.

17. The method according to any one of claims 1 to 3 or 6 to 16, wherein the subjects opioid use is reduced by about 20%, about 30%, about 40% relative to their baseline opioid use prior to administering the composition.

18. The method according to any one of claims 1 to 3 or 6 to 17, wherein the subjects mean VAS score is reduced relative to their VAS score prior to administering the composition.

19. The method according to any one of claims 1 to 3 or 6 to 18, wherein the subjects visual analog scale (VAS) pain response is 30%, preferably 50%.

20. The method according to any one of claims 1 to 3 or 6 to 19 or the composition according to any one of claims 5 to 19, wherein the opioid is morphine.

21. The method according to any one of claims 1 to 3 or 6 to 20, wherein the subjects mean EQ-5D score is increased from baseline.

22. The method according to any one of claims 2 to 3 or 6 to 20, wherein the subject achieves a ODI 10 point function response, preferably a 15 point ODI function response.

23. The method according to any one of claims 1 to 3 or 6 to 22, wherein the subject has no significant pain 12 months, preferably 24 months after administering the composition.

24. The method according to any one of claims 1 to 3 or 6 to 23, wherein the subject discontinues opioid use 12 months to 24 months after administering the composition.

25. The method according to any one of claims 1 to 3 or 6 to 24, wherein the subject has an ODI score between 25 and 70%, between 30 and 60%.

26. The method according to any one of claims 1 to 3 or 6 to 25 or the composition according to any one of claims 5 to 15, wherein the MLPSCs are STRO-1+.

27. The method according to any one of claims 1 to 3 or 6 to 26 or the composition according to any one of claims 5 to 15 or 26, wherein the MLPSCs are mesenchymal stem cells (MSCs).

28. The method according to any one of claims 1 to 3 or 6 to 27 or the composition according to any one of claims 5 to 15 or 26 or 27, wherein the cells are allogeneic and/or culture expanded, preferably, wherein the cells are TNAP+ before they are culture expanded.

29. The method according to any one of claims 1 to 3 or 6 to 28 or the composition according to any one of claims 5 to 15 or 25 to 28, wherein the cells have been cryopreserved.

30. The method according to any one of claims 1 to 3 or 6 to 29, which comprises administering between 1×10^7 and 2×10^8 cells.

31. The composition according to any one of claims 5 to 15 or 25 to 29, which comprises between 1×10^7 and 2×10^8 cells.

32. The method according to any one of claims 1 to 3 or 6 to 30 or the composition according to any one of claims 5 to 15 or 25 to 29 or 31, wherein the composition comprises human bone marrow-derived allogeneic mesenchymal precursor cells (MPCs) isolated from bone mononuclear cells with anti-STRO-3 antibodies, expanded *ex vivo*, and cryopreserved.

33. The method according to any one of claims 1 to 3 or 6 to 32 or the composition according to any one of claims 5 to 15 or 25 to 29 or 31 or 32, wherein the subject has been experiencing pain for between 6 and 68 months.

34. The method according to any one of claims 1 to 3 or 6 to 33 or the composition according to any one of claims 5 to 15 or 25 to 29 or 31 to 33, wherein the subject has not been experiencing pain for more than 68 months.

35. The method according to any one of claims 1 to 3 or 6 to 33 or the composition according to any one of claims 5 to 15 or 25 to 29 or 31 to 34, wherein the pain is axial pain.

36. The method or composition according to claim 35, wherein the axial pain is due to nerve root compression defined by MRI.

37. The method according to any one of claims 1 to 3 or 6 to 36, wherein the subject discontinues opioid use 36 months after administering the composition.

38. The composition according to any one of claims 5 to 15 or 25 to 29 or 31 to 34, wherein the composition discontinues opioid use in a subject 36 months after administration.

39. Use of a composition according to any one of claims 5 to 15 or 25 to 29 or 31 to 34 in the manufacture of a medicament for discontinuing opioid use by a subject, wherein the opioid use is discontinued 36 months after administration of the composition.

40. Use of claim 39, wherein the subject has chronic pain.

41. Use of claim 40, wherein the subject has chronic lower back pain.

CLAIMS

1. Use of a composition comprising mesenchymal lineage precursor or stem cells (MLPSCs) in the manufacture of a medicament for reducing opioid use in a subject, in which the subject is using an opioid.

2. Use according to Claim 1, in which the composition comprises hyaluronic acid (HA).

3. Use according to Claim 1 or 2, in which the subject is using an opioid for pain.

4. Use according to Claim 1, 2 or 3, in which of the pain is chronic pain.

5. Use according to Claim 1, 2 or 3, in which pain is lower back pain, preferably in which the lower back pain is associated with a degenerated disc.

6. Use according to Claim 5, in which the lower back pain is non-radicular in origin and/or is associated with one or more of:

an intervertebral disc herniation up to a 3mm protrusion;

nerve ingrowth into an intervertebral disc; and

inflammation in an intervertebral disc.

7. Use according to Claim 6, in which the nerve ingrowth or inflammation is in the intervertebral disc space, or the nucleus pulposus, or the annulus fibrosis of the intervertebral disc.

8. Use according to any preceding claim, in which opioid use is reduced between 1 and 3 months after administration of the composition.

9. Use according to any of Claims 1 to 7, in which opioid use is reduced for at least 12 months after administration of the composition.

10. Use according to any of Claims 1 to 8, in which opioid use is reduced relative to the subject's average baseline morphine equivalent dose prior to administering the composition.

11. Use according to any preceding claim, in which the subject has been using an opioid for at least 1 to 6 months prior to administering the composition.

12. Use according to any preceding claim, in which the opioid is morphine.

13. Use according to any preceding claim, in which the subject's opioid use is reduced by between 20% and 40% relative to their baseline opioid use prior to administering the composition.

14. Use according to any preceding claim, in which the subject discontinues opioid use between 12 months and 24 months after administering the composition.

15. Use according to any preceding claim, in which the MLPSCs are STRO-1+.

16. Use according to any of Claims 1 to 14, in which the MLPSCs are mesenchymal stem cells (MSCs).

17. Use according to any of Claims 3 to 16, in which the subject's mean EQ-5D score is increased from baseline after administering the composition.

18. Use according to any of Claims 3 to 17, in which the subject achieves a ODI 10 point function response, preferably a 15 point ODI function response after administering the composition.

19. Use of a composition comprising mesenchymal lineage precursor or stem cells (MLPSCs) in the manufacture of a medicament for reducing pain, in which the subject is using an opioid.

20. Use of a composition comprising mesenchymal lineage precursor or stem cells (MLPSCs) in the manufacture of a medicament for reducing pain and/or increasing EQ-5D score, in which the subject is using an opioid.

21. An opioid sparing composition comprising mesenchymal lineage precursor or stem cells (MLPSCs) and 1% hyaluronic acid (HA).