CLAIMS

What is claimed is:

1. Use of a therapeutic composition in the manufacture of a medicament for treating a dry eye disease, wherein the therapeutic composition is obtained by:

differentiating an *ex-vivo* culturing of a population of induced pluripotent stem cells (iPSCs) into mature megakaryocyte-like cells (MLCs);

lysing the mature MLCs to produce lysates;

processing the lysates to form the therapeutic composition, wherein the therapeutic composition comprises factors of one or more of: epidermal growth factor (EGF)>10% higher or interleukin (IL)-10>10% higher as compared to plasma rich in growth factors (PRGF), and EGF>10% higher, IL-10>10% higher as compared to crude lysates; and

wherein an effective amount of the therapeutic composition is to be administered to a subject suffering from the dry eye disease, thereby treating the dry eye disease.

2. The use of claim 1, wherein the lysates comprise factors of one or more of: EGF>50% higher or IL-10>50% higher as compared to PRGF.

3. The use of claim 1, wherein the lysates comprise factors of one or more of: matrix metalloproteinase (MMP)-1>10% higher, MMP-9>10% higher, MMP-12, tissue inhibitors of metalloproteinases (TIMP)-1>10% higher, TIMP-3>10% higher, transforming growth factors (TGF)-B1>10% higher, TGF-B2>10% higher, Endoglin>10% higher, Endothelin-3>10% higher, Follistatin>10% higher, heparin-binding (HB)-EGF>10% higher, hepatocyte growth factor (HGF) >10% higher, placental growth factor (PLGF) >10% higher, vascular endothelial growth factor (VEGF)-A>10% higher, soluble CD40L (sCD40L) >10% higher, Eotaxin>10% higher, fibroblast growth factors (FGF)-2>10% higher, FLT-3L>10% higher, Fractalkine>10% higher, granulocyte colony stimulating factor (G-CSF) >10% higher, growth-regulated oncogene a (GROa) >10% higher, interferon (IFN)-a2>10% higher, IFNy>10% higher, IL-1a>10% higher, IL-1B>10% higher, IL-1RA>10% higher, IL-2>10% higher, IL-3>10% higher, IL-4>10% higher, IL-5>10% higher, IL-6>10% higher, IL-8>10% higher, IL-9>10% higher, IL-10>10% higher, IL-12p40>10% higher, IL-12p70>10% higher, IL-13>10% higher, IL-15>10% higher, IL-17A>10% higher, IL-17E>10% higher, IL-25>10% higher, IL-17F>10% higher, IL-22>10% higher, IL-27>10% higher, interferon gamma-induced protein (IP)-10>10% higher, monocyte chemoattractant protein (MCP)-1>10% higher, MCP-3>10% higher, macrophage-derived chemokine (MDC) >10% higher, macrophage inflammatory

protein (MIP)-1a>10% higher, MIP-1b>10% higher, platelet-derived growth factor (PDGF)-AA>10% higher, transforming growth factor (TGF) a>10% higher, tumor necrosis factor (TNF) a>10% higher, TNFB>10% higher, a proliferation-inducing ligand (APRIL) >10% higher, B-cell activating factor (BAFF)>10% higher, regulated upon activation, normal T cell expressed and secreted (RANTES)>10% lower, IL-7>10% lower, VEGF-D>10% lower, VEGF-C>10% lower, Leptin>10% lower, angiopoietin (Ang) 2>10% lower, transforming growth factor (TGF) B-3>10% lower, MMP-10>10% lower, MMP-7>10% lower, MMP-3>10% lower, or MMP-2>10% lower as compared to PRGF as compared to PRGF.

4. The use of claim 1, wherein the lysates comprise factors of one or more of: MMP-7>10% higher, TIMP-1>10% higher, TIMP-3>10% higher, IL-2>10% higher, IL-15>10% higher, IL-17F>10% higher, granulocyte colony stimulating factor (G-CSF)>10% higher, MMP-13>10% lower, TGFB-1>10% lower, IL-5>10% lower, APRIL>10% lower, or BAFF>10% lower as compared to crude lysates.

5. The use of claim 1, wherein one or more signs and/or symptoms of dry eye disease is improved.

6. The use of claim 1, wherein the dry eye disease is caused by Sjogren’s syndrome or non-Sjogren’s syndrome.

7. The use of claim 1, wherein the therapeutic composition is diluted to a physiological concentration in a carrier, wherein the carrier comprises a diluent or an excipient.

8. The use of claim 1, wherein the therapeutic composition further comprises a wound healing agent, a tissue regeneration agent, an antiapoptotic agent, an anti-inflammatory agent, a neurotropic agent, an anti-hormonal agent or an immunomodulatory agent or a combination thereof.

9. The use of claim 8, wherein the tissue regeneration agent is one or more of (a) a growth factor selected from one or more of transforming growth factors (TGF), fibroblast growth factors (FGF), platelet-derived growth factors (PDGF), epidermal growth factors (EGF), vascular endothelial growth factors (VEGF), insulin-like growth factors (IGF), platelet-derived endothelial growth factors (PDEGF), platelet-derived angiogenesis factors (PDAF), platelet factors 4 (PF-4), hepatocyte growth factors (HGF) or combinations thereof; and (b) a cytokine

selected from one or more of IL-1B, IL-5, IL-6, IL-8, IL-10, IL-12, IL-13, IL-17A, IL-23, TNF alpha or combinations thereof.

10. The use of claim 1, wherein the population of cells comprises cells derived from immortalization, reprogramming or differentiation of a somatic cell, a progenitor cell or a stem cell.

11. The use of claim 1, wherein the therapeutic composition further comprises lysates, serum, plasma, plasma rich in growth factors (PRGF), platelet rich plasma (PRP), or any other blood derivative derived from the subject.

12. The use of claim 1, wherein the therapeutic composition in formulated in a buffer, diluent, or excipient or a combination thereof.

13. The use of claim 1, wherein the therapeutic composition comprises: a) between 0.01 and 100 wt % of the lysates, b) between 0 and 90 wt. % of a bulking agent, and/or c) between 0 and 90 wt. % of at least one excipient or carrier and optionally d) platelet-rich plasma (PRP), PRGF, plasma, serum, or other blood derivative derived from the subject.

14. The use of claim 1, wherein the therapeutic composition is lyophilized.

15. The use of claim 1, wherein the therapeutic composition is to be locally administered at one or more of a site of or near an injury or a disease,

wherein the therapeutic composition is to be administered by any one of route of administrations selected from topical, transdermal, or systemic route of administration, or

wherein the therapeutic composition is to be administered by any one of route of administrations selected from subconjunctival, sub-Tenon's, intravitreal, intracameral, intravenous, intraarterial, intramuscular, subcutaneous, inhalation, rectal, buccal, vaginal, intraperitoneal, intraarticular, intraglandular into a lacrimal gland, topical, otic, or oral route of administration.

16. Use of a therapeutic composition in the manufacture of a medicament for treating a dry eye disease, wherein an effective amount of the therapeutic composition is to be administered to a subject suffering from the dry eye disease, wherein the therapeutic composition comprises lysates of megakaryocyte-like cells (MLCs), wherein, after processing, the lysates comprise factors of one or more of: epidermal growth factor (EGF)>10% higher or interleukin (IL)-

10>10% higher as compared to plasma rich in growth factors (PRGF), and EGF>10% higher, IL-10>10% higher as compared to crude lysates.

17. A method for producing a therapeutic composition comprising an effective amount of processed lysates of MLCs, the method comprising:

an *ex-vivo* culturing of a population of iPSCs for a duration to differentiate the iPSCs to mature MLCs;

concentrating the MLCs;

lysing the MLCs; and

processing the lysed MLCs to form the therapeutic composition;

wherein, after processing, the therapeutic composition comprises factors of one or more of: epidermal growth factor (EGF)>10% higher or interleukin (IL)-10>10% higher as compared to plasma rich in growth factors (PRGF), and EGF>10% higher, IL-10>10% higher as compared to crude lysates.

18. The method of claim 17, wherein the processing comprises filtering the lysed MLCs.

19. The method of claim 17, wherein the processing comprises centrifuging the lysed MLCs.

20. A therapeutic composition for treating a dry eye disease in a subject, the therapeutic composition comprising an effective amount of an MLC lysate, wherein the MLC lysate comprise factors of one or more of: epidermal growth factor (EGF)>50% higher or interleukin (IL)-10>50% higher as compared to plasma rich in growth factors (PRGF), and EGF>50% higher, IL-10>50% higher as compared to crude lysates.

21. The therapeutic composition of claim 20, wherein the MLC lysate comprises one or more biomarkers selected from fibroblast growth factor-2 (FGF-2); hepatocyte growth factor (HGF); insulin-like growth factor 1 (IGF-1), regulated upon activation, normal T cell expressed and secreted (RANTES); nerve growth factor (NGF); vascular endothelial growth factor (VEGF-A); vascular endothelial growth factor (VEGF-C); epidermal growth factor (EGF); transforming growth factor-β1 (TGF-β1); transforming growth factor-β2 (TGF-β1); platelet-derived growth factor-AA (PDGF-AA); platelet-derived growth factor-BB (PDGF-BB); platelet-derived growth factor-AA/BB (PDGF-AA/BB); interleukin 2 (IL-2); interleukin 4 (IL-4); interleukin 12p40 (IL-12p40); interleukin 12p70 (IL-12p70); tissue inhibitors of

metalloproteinases-1 (TIMP-1); tissue inhibitors of metalloproteinases-2 (TIMP-2); and tissue inhibitors of metalloproteinases-3 (TIMP-3).

22. The therapeutic composition of claim 20, wherein the therapeutic composition further comprises another therapeutic agent.