Claims

1. Use of a population of cells in the manufacture of a composition for treating a subject having diabetes, wherein the population comprises a plurality of cells that express ISL1;

wherein the composition comprises about 1 x 10^8 to about 10 x 10^8 cells; wherein the composition comprises NKX6.1$^+$/ISL1$^+$ cells that will display a GSIS in vivo; wherein the subject has been treated with one or more immunosuppression-induction agents between 3 and 35 days prior to treatment with the composition.

2. The use of claim 1, wherein the subject has been treated with one or more immunosuppression-induction agents between 6-28 or 10-21 days prior to treatment with the composition.

3. The use of claim 1 or 2, wherein the immunosuppression-induction agent is an anti-thymocyte globulin binding moieties (e.g., ATG-R, ATG-F, ATGAM), an anti-CD3 binding moiety (e.g., OKT3), an anti-CD25 binding moiety (e.g., daclizumab or basiliximab), an anti-CD52 binding moiety (e.g., alemtuzumab), or a high dose of an immunosuppression maintenance agent (e.g., bolus glucocorticosteroids or intravenous cyclosporine [CsA]).

4. The use of any one of claims 1-3, wherein the immunosuppression-induction agent is an anti-thymocyte globulin binding moiety.

5. The use of any one of claims 1-4, wherein the subject has been treated with 1, 2, 3, 4, 5, 6, 7, 8, or 9 doses of the immunosuppression-induction agent prior to treatment with the composition.

6. The use of any one of claims 1-5, wherein the subject has been treated with 1, 2, or 3 doses of the immunosuppression-induction agent on a first day, and has then be treated with 1, 2 or 3 doses of the immunosuppression-induction agent on a second day (e.g., 1-35, 1-28, 1-21, 1-14, 1-7, 1-5, 1-3, 1-2, or 1 day after the administration of the doses of the immunosuppression-induction agent on the first day).

7. The use of any one of claims 1-6, wherein the subject has been treated with 1, 2, or 3 doses of the immunosuppression-induction agent prior to treatment with the composition, and wherein the subject is to be treated with 1, 2 or 3 doses of an immunosuppression-induction agent within 1, 2, or 3 days after treatment with the composition.

8. The use of any one of claims 1-7, wherein the subject is to be treated with sirolimus and/or tacrolimus after treatment with the composition.

9. The use of any one of claims 1-8, wherein the subject is to be treated with mycophenolate mofetil or mycophenolate sodium after treatment with the composition.

10. The use of any one of claims 1-9, wherein:

a. 35-60% of the cells in the composition express C-peptide and ISL1 but not VMAT1;

b. 4-25%, of the cells in the composition express glucagon but not somatostatin; and

c. 1-10% of the cells in the composition express somatostatin but not glucagon.

11. The use of any one of claims 1-10, wherein no less than 50%, 40%, 30%, or 20% of the cells in the composition are $NKX6.1^{+}/ISL1^{+}$ cells, as determined by flow cytometry.

12. The use of any one of claims 1-11, wherein no less than 40%, 35%, 30%, 26 %, 25%, or 20% of the cells in the composition are $NKX6.1^{-}/ISL1^{+}$ cells, as determined by flow cytometry.

13. The use of any one of claims 1-12, wherein between 20-60%, 20-50%, 20-45%, 20-40%, 20-35%, 20-30%, 20-25%, 25-50%, 25-40%, 25-35%, 30-60%, 30-50%, 30-40%, 30-35%, 35-50%, 40-50% of the cells in the composition are $NKX6.1^{+}/ISL1^{+}$ cells, as determined by flow cytometry.

14. The use of any one of claims 1-13, wherein between 20-60%, 20-50%, 20-45%, 20-40%, 20-35%, 20-30%, 20-25%, 25-50%, 25-40%, 25-35%, 30-60%, 30-50%, 30-40%, 30-35%, 35-50%, or 40-50% of the cells in the composition are $NKX6.1^{-}/ISL1^{+}$ cells, as determined by flow cytometry.

15. The use of any one of claims 1-14, wherein less than 6% or between 0-6%, 0-4%, 0-2%, 0-1%, 1-6%, 1-5%, 1-4%, 1-3%, 1-2%, 2-3%, or 3-6% of the cells in the composition are $NKX6.1^{-}/ISL1^{-}$ cells, as determined by flow cytometry.

16. The use of any one of claims 1-15, wherein the composition comprises $NKX6.1^{+}/ISL1^{+}$ cells that display a GSIS in vitro.

17. The use of any one of claims 1-16, wherein the population of cells are generated from stem cells *in vitro*.

18. The use of any one of claims 1-17, wherein at least a portion of the cells in the population of cells are present in plurality of cell clusters.

19. The use of claim 18, wherein the cell clusters are about 50 μm to about 500 μm, about 50 μm to about 400 μm, about 50 μm to about 300 μm, about 60 μm to about 400 μm, about 60 μm to about 300 μm, about 60 μm to about 250 μm, about 75 μm to about 400 μm, about 75 μm to

about 300 μm, about 75 μm to about 250 μm, about 125 μm to about 225 μm, about 130 μm to about 160 μm, about 170 μm to about 225 μm, about 140 μm to about 200 μm, about 140 μm to about 170 μm, about 160 μm to about 220 μm, about 170 μm to about 215 μm, or about 170 μm to about 200 μm in diameter.

20. The use of any one of claims 1-19, wherein the composition comprises a plurality of NKX6.1-positive; ISL1-positive cells, wherein the NKX6.1-positive; ISL1-positive cells express higher (e.g., at least 10%, 30%, 50%, 70%, 100%, 125%, 150%, or 200% higher) levels of MAFB, CHGA, ESRRG, SIX2, HOPX, IAPP and/or UCN3 than NKX6.1-positive; ISL1-positive cells from the pancreas of a healthy control adult subject.

21. The use of any one of claims 1-20, wherein the composition comprises a plurality of NKX6.1-positive; ISL1-positive cells, wherein the NKX6.1-positive; ISL1-positive cells express SIX3, MAFA, CHGB, RBP4 and/or FXYD2 at a lower (e.g., at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or 100% lower) level than a NKX6.1-positive, ISL1-positive cell from the pancreas of a healthy control adult subject.