## Claims

What is claimed is:

1. A method of manufacturing a cellular therapy product, wherein the cellular therapy product comprises a first cellular surface receptor which is able to bind to a drug target molecule on the surface of a drug target cell, and/or wherein the cellular therapy product produces and/or secretes a polypeptide which is able to bind to a drug target molecule either soluble or associated with a drug target cell, comprising

   a) enriching via reversible immobilization in a holding step a cellular therapy starting cell obtained from a sample comprising the cellular therapy starting cell, using at least one second cellular surface receptor of the cellular therapy starting cell, and wherein the second cellular surface receptor of the cellular therapy starting cell is specifically bound by a monovalent or divalent receptor binding reagent, and

   b) genetically modifying the cellular therapy starting cell using one or more reagent(s) for genetic modification comprising a gene construct for expression of the first cellular surface receptor and/or for expression and/or secretion of the polypeptide, thereby generating a precursor of the cellular therapy product,

   wherein the method takes place in a closed system, wherein the cellular therapy starting cell is a non-activated lymphocyte, wherein the one or more reagent(s) for genetic modification comprises a non-viral gene delivering system.

2. The method of claim 1, further comprising c) formulating the precursor of the cell therapy product in a buffer suitable for subsequent administration of the precursor of the cellular therapy product to a patient.

3. The method of any of claims 1 or 2, wherein the duration of the method is between about 1.5 hours to about 16 hours.

4. The method of any of the preceding claims, wherein the sample comprises a bodily fluid, preferably wherein the sample comprises nucleated blood cells, more

preferably wherein the sample is a whole blood sample or wherein the sample comprises or consists of white blood cells.

5. The method of any one of the preceding claims, wherein the cellular therapy starting cell is a non-activated T cell, a non-activated B cell or a non-activated NK cell.

6. The method of any of the preceding claims, wherein the drug target cell is a diseased cell, preferably in an infectious disease or a cancer cell or an autoreactive cell causing an autoimmune disease.

7. The method of any of the preceding claims, wherein enriching via reversible immobilization of the cellular therapy starting cell from the sample comprises

- providing the sample, the sample comprising the cellular therapy starting cell,
- providing the receptor binding reagent comprising a binding site B and a binding partner C,
- wherein the binding site B comprised in the receptor binding reagent is capable of specifically binding to the second cellular surface receptor on the cellular therapy starting cell and wherein the bond between the binding site B of the receptor binding reagent and the second cellular surface receptor has a dissociation constant ($K_D$) from about $10^{-7}$ to about $10^{-10}$ M,
- wherein the binding partner C comprised in the receptor binding reagent is capable of reversibly binding to a binding site Z of an affinity reagent and the reversible bond between the binding partner C of the receptor binding reagent and the binding site Z of the affinity reagent has a dissociation constant ($K_D$) in the range from about $10^{-2}$ to about $10^{-13}$ M, and
- exposing the sample to chromatography on a suitable solid phase, for example, floating particles or a stationary phase, the solid phase, for example, the solid phase and/or the stationary phase having the affinity reagent immobilized thereon,
- wherein the affinity reagent comprises one or more binding sites Z, wherein said binding site Z forms a reversible bond with the binding partner C comprised in the receptor binding reagent, and wherein the binding site B of the receptor binding reagent binds to the second cellular surface receptor on

the cellular therapy starting cell, thereby reversibly immobilizing the cellular therapy starting cell on the solid phase,

- providing a competition reagent, the competition reagent comprising a binding site, specifically binding to the binding sites Z of the affinity reagent;
- loading the competition reagent onto the stationary phase, thereby allowing disruption of non-covalent reversible complexes formed between (a plurality of) the receptor binding reagent, the second cellular surface receptor and the affinity reagent;
- recovering an enrichment sample from the eluate of the stationary phase, wherein the enrichment sample comprises the cellular therapy starting cell.

8. The method of claim 7, wherein the receptor binding reagent is selected from the group of an immunoglobulin, a functional fragment of an immunoglobulin, a proteinaceous binding molecule with immunoglobulin-like functions, an aptamer and an MHC molecule.

9. The method of any one of claims 7 or 8, wherein the binding partner C comprised in the receptor binding reagent comprises one of biotin, a biotin analogue, a streptavidin binding peptide and an avidin binding peptide, and wherein the affinity reagent comprises streptavidin, a streptavidin mutein, avidin an avidin mutein or a mixture thereof, preferably wherein the streptavidin mutein includes the amino acid sequence $Val^{44}$-$Thr^{45}$-$Ala^{46}$-$Arg^{47}$ (SEQ ID NO. 7) or $Ile^{44}$-$Gly^{45}$-$Ala^{46}$-$Arg^{47}$ (SEQ ID NO. 8) in the region of the amino acid positions 44 to 47 with reference to the amino acid sequence of wild type streptavidin as set forth in SEQ ID NO. 9.

10. The method of any one of claims 7 or 8, wherein the binding partner C comprised in the receptor binding reagent comprises an affinity tag, and wherein the affinity reagent comprises a suitable binding partner for the affinity tag, preferably an antibody or an antibody fragment, which is capable of binding to the affinity tag, preferably wherein the affinity tag is selected from a group comprising an oligohistidine, a polyhistidine, an immunoglobulin domain, a maltose-binding protein, a glutathione-S-transferase (GST), a chitin binding protein (CBP), a

thioredoxin, a calmodulin binding peptide (CBP), a FLAG'-peptide, a HA-tag, a VSV-G-tag, and a HSV-tag.

11. The method of any one of claims 7 to 10, wherein the stationary phase is comprised in a reservoir such as bag, a tubing, a column or is a planar stationary phase.

12. The method of any one of claims 7 to 11, wherein the stationary phase or the solid phase comprises or consists of one of a plastic tubing, a cellulose membrane, a plastic membrane, a polysaccharide gel, a polyacrylamide gel, an agarose gel, polysaccharide grafted silica, polyvinylpyrrolidone grafted silica, polyethylene oxide grafted silica, poly(2-hydroxyethylaspartamide) silica, poly(N-isopropylacrylamide) grafted silica, polystyrene particles, a styrene-divinylbenzene gel, a copolymer of an acrylate or an acrylamide and a diol, a co-polymer of a polysaccharide and N,N'-methylenebisacrylamide and a combination of any two or more thereof.

13. The method of any of preceding claims, wherein the second cellular surface receptor on the cellular therapy starting cell is selected from the group of CD3, CD4, CD8, CD45, CD56, CD27, CD28, CD19, CD62L, CD25.

14. The method of any of the preceding claims 7 to 12, wherein the reversible immobilization is carried out via two or more types of the second cellular surface receptor, for example, by sequential immobilization via the cell surface receptor CD3 as first type of second cellular surface receptor and CD4 as second type of second cell surface receptor.

15. The method of any of the preceding claims, wherein enriching via reversible immobilization of the cellular therapy starting cell is carried out as single enrichment step, without prior cell separation, in particular without prior cell separation in a cell separation module comprising a cell separator configured to produce a fraction enriched in nucleated blood cells.

16. The method of any of the preceding claims, wherein the non-viral gene delivering system comprises an electroporation, a lipid nanoparticle, mechanoporation, ultrasound treatment, optical gene delivery, exosomes, amphiphilic peptides or a combination thereof, wherein a lipid nanoparticle is preferred.

17. The method of claim 16, wherein the reagent(s) for genetic modification comprises a nucleic acid encoding a Transcription activator-like effector nuclease (TALEN), a Zinc-finger nuclease (ZFN), or CRISPR and Cas, transposases such as sleeping beauty, piggyback, Tn5 transposases or wherein the set of reagents comprises a Transcription activator-like effector nuclease (TALEN), a Zinc-finger nuclease (ZFN), or CRISPR and Cas, and/or wherein the reagent(s) for genetic modification comprises the gene construct comprising a nucleic acid encoding the first cellular surface receptor and/or the polypeptide, wherein the nucleic acid can be DNA or mRNA, preferably wherein the gene construct comprises a nucleic acid encoding a chimeric antigen receptor (CAR), a recombinant T cell receptor (TCR), switch receptors, which is able to bind to the drug target molecule.

18. The method of any one of the claims 16 to 17, wherein the gene modification takes place before or after eluting the cellular therapy starting cell from the stationary phase.

19. The method of any one of the preceding claims, wherein the sample is a whole blood sample, the cellular therapy starting cell is the non-activated T cell and the reagent(s) for genetic modification comprises the non-viral gene delivering system, the nucleic acid encoding the CRISPR and Cas, and the nucleic acid encoding the chimeric antigen receptor (CAR) or the TCR, which is able to bind to the drug target molecule, or wherein the sample is a whole blood sample, the cellular therapy starting cell is the non-activated B cell and the reagent(s) for genetic modification comprises the non-viral gene delivering system, the nucleic acid encoding the CRISPR and Cas, and the nucleic acid encoding the polypeptide or wherein the sample is a whole blood sample, the cellular therapy starting cell is the non-activated T cell, B cell or NK cell and the reagent(s) for genetic modification comprises the non-viral gene delivering system comprising the lipid nanoparticle.