

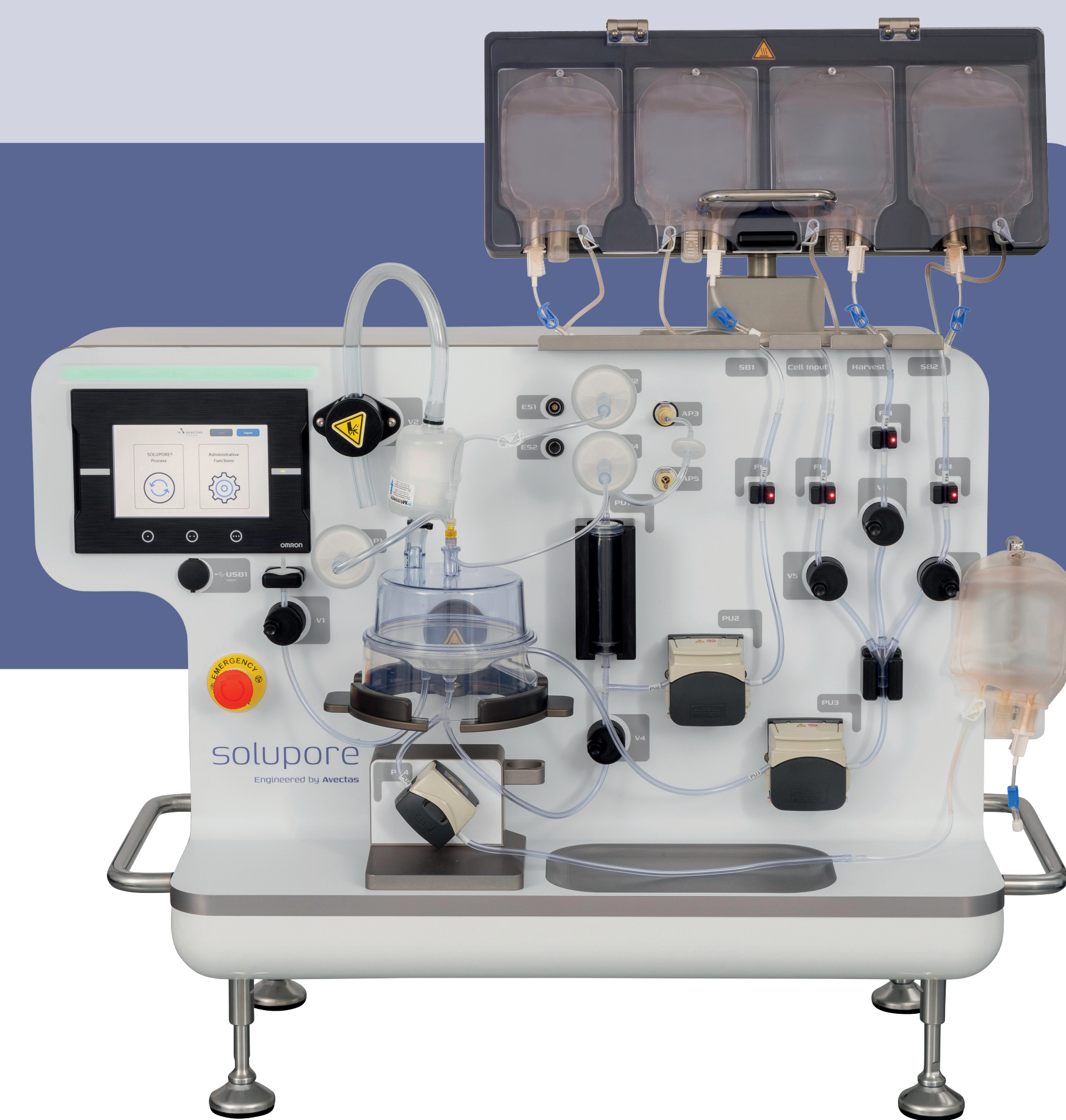
A scalable, rapid & automated manufacturing platform, Solupore®, a flexible offering for both autologous and allogeneic cell therapies

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INTRODUCTION

Cell therapies have shown remarkable clinical success in treating haematological malignancies, and attention is now turning to their potential in non-oncology applications such as autoimmune diseases. However, the cost and scalability of manufacturing processes to support the delivery of these cell therapies to patients remains a significant industry challenge. Avectas is developing a new manufacturing platform designed to integrate the manufacturing steps of gene-edited cells, including CAR-T cells. For edited cells, this platform enables key manufacturing steps, including cell activation, viral transduction, non-viral transfection and expansion, to occur within a single-use, GMP (Good Manufacturing Practice) aligned, closed system.

In this study, we present the capabilities of the Solupore® Integrated Single Use System in supporting end-to-end CAR-T manufacturing, enabling non-viral transfection/gene editing, CD19-CAR lentiviral transduction and expansion to clinically relevant numbers of cells, while maintaining cell health and function (**Figure 1**). By reducing manufacturing complexity and cost, Solupore® aims to enable the scalable production of potent gene-modified cell therapies for the benefit of patients.



SOLUPORE SUS: INTEGRATED MANUFACTURING SOLUTION FOR CELL THERAPY

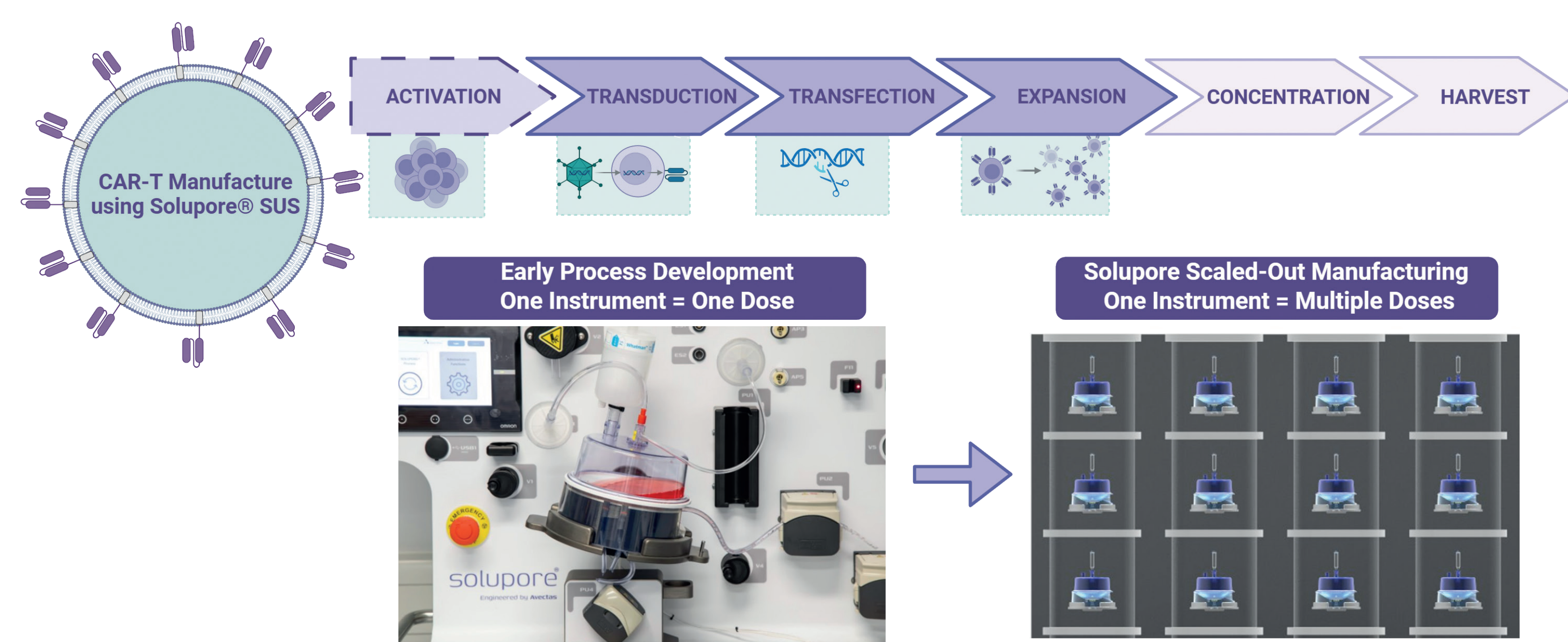


Figure 1: Solupore® integrated Single Use System (SUS) offers an end-to-end solution for next generation CGT manufacturing which can support T cell activation, transduction, non-viral transfection and expansion within a single consumable. Future development aims to deliver a Solupore instrument which manufactures multiple doses in parallel.

RESULTS SUMMARY

Solupore SUS supports Non-Viral Transfection & Expansion at Scale

- Solupore® is a non-viral transfection technology which has been adapted to enable rapid, large-scale cell processing using a flow-through system (FTS), as well as integrated expansion of the resulting cell product, within a single consumable (**Figure 2A**).
- CD3 T cells (48×10^6) were transfected using Solupore® FTS resulting in $52.6 \pm 2\%$ KO efficiency (CRISPR/Cas9 RNP-based target TRAC) (**Figure 2B**, n=2 donors). Solupore transfected cells showed equivalent levels of healthy, non-apoptotic cells to an untransfected (UT) control (**Figure 2D**, n=2).
- The resulting cell product was then expanded using Avectas' integrated single-use manufacturing system (SUS) (**Figure 2A**), yielding $6.2 - 8.6 \times 10^8$ total live cells at Day 10 (**Figure 2C**, n=2 donors) and eliminating the need for an external TC flask or bioreactor.

Solupore SUS supports Large-Scale Integrated CAR-T Manufacture

- Solupore SUS can also support CAR-T viral transduction and expansion to clinical-scale (**Figure 3**).
- Following 1-day T-flask activation, CD3 T cells (50×10^7) were transduced with a CD19-CAR lentiviral vector (MOI 1) using Solupore SUS and expanded for 10 days (**Figure 3A**). Consistent CAR-T cell fold growth was observed over 10 days, yielding $>1 \times 10^9$ total live cells with $>30\%$ CAR+ efficiency & $>80\%$ viability (**Figure 3B-C**, n=2 donors).

CAR-T Cell Function & Phenotype

- CD19-CAR-T cells manufactured using Solupore SUS have a higher target cell killing capacity compared to non-transduced (Non-T) negative controls (**Figure 4A**) and retain early memory T cell subsets (central/stem cell memory phenotype), which correlate with better persistence in vivo (**Figure 4B**).

SOLUPORE SUS SUPPORTS NON-VIRAL TRANSFECTION & EXPANSION AT SCALE

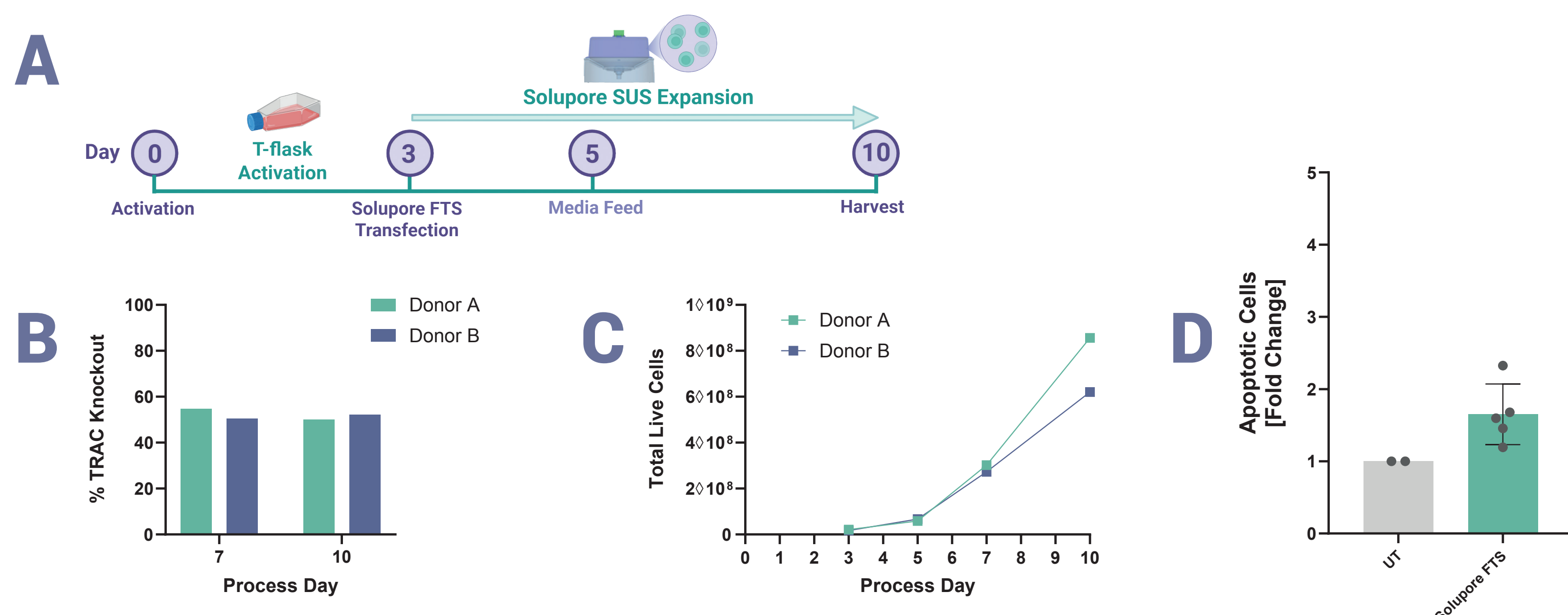


Figure 2: (A) Transfection and expansion process using Solupore SUS. (B) CRISPR/Cas9 TRAC KO efficiency at Day 7-10 (n=2 donors) following Solupore FTS transfection. (C) Post-transfection, the resulting cell product was expanded using Solupore SUS, yielding $6.2 - 8.6 \times 10^8$ total live cells at Day 10 (n=2 donors). (D) Apoptosis was measured 30 min post-Solupore FTS transfection compared to untransfected (UT) cells (Fold change, n=2 donors).

SOLUPORE SUS SUPPORTS LARGE-SCALE INTEGRATED CAR-T MANUFACTURE

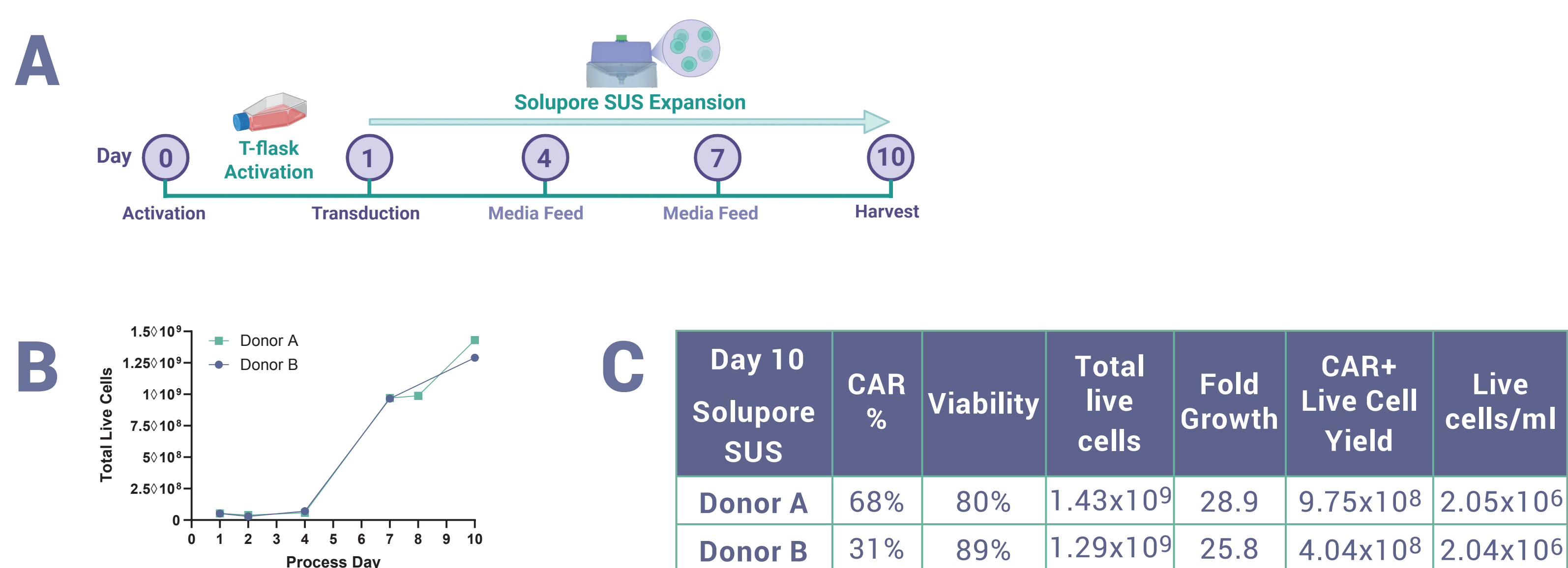


Figure 3: (A) CAR-T cell manufacturing process using Solupore SUS. (B-C) 1-day post-activation in a T-flask (with TransACT™), T cells were transduced with a second generation CD19-CAR lentiviral vector (MOI 1) and expanded for 10 days using the Solupore SUS platform. Consistent CAR-T cell fold growth for two donors was observed over 10 days in TCM media + IL-2, yielding $>1 \times 10^9$ total live cells on Day 10 with $>30\%$ CAR+ efficiency and $>80\%$ viability.

T CELL FUNCTION & PHENOTYPE

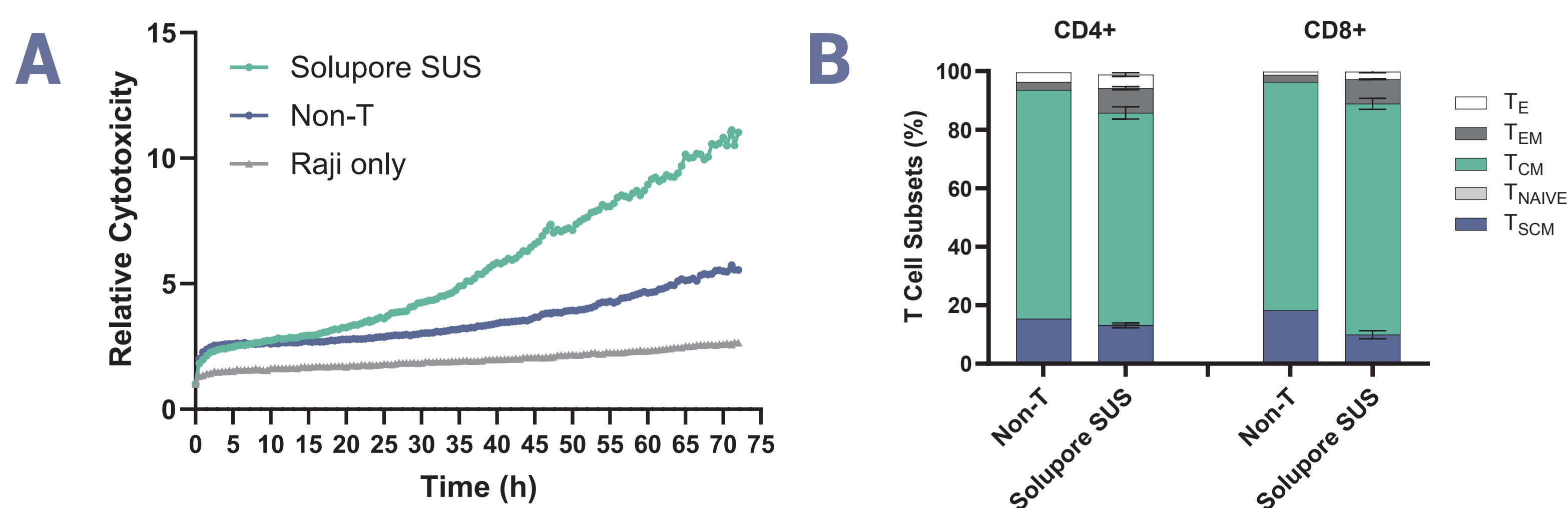


Figure 4: (A) CD19-CAR cells manufactured using Solupore SUS have a higher target cell (CD19+ Raji cells) killing capacity compared to non-transduced (non-T) negative controls. Representative figure for 1:1 ratio. Data displayed as mean only. (B) T cell phenotype of Solupore SUS manufactured CAR-T cells at 7 days post-activation compared to non-transduced control.

DISCUSSION & CONCLUSION

This study demonstrates how the Solupore® integrated Single Use System can support both non-viral transfection/gene editing (**Figure 2**) and CAR-T cell transduction (**Figure 3**), as well as integrated expansion of the resulting cell product to generate clinically relevant numbers of cells, within a single consumable.

This scalable, GMP-ready, immune cell therapy manufacturing solution can process large cell numbers ($10^8 - 10^9$), to support end-to-end autologous CAR-T manufacturing, while maintaining cell health, function and potency.

Future development aims to deliver a Solupore platform that manufactures multiple doses in parallel, supporting the cost-effective production of potent high quality therapeutic cell products.

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