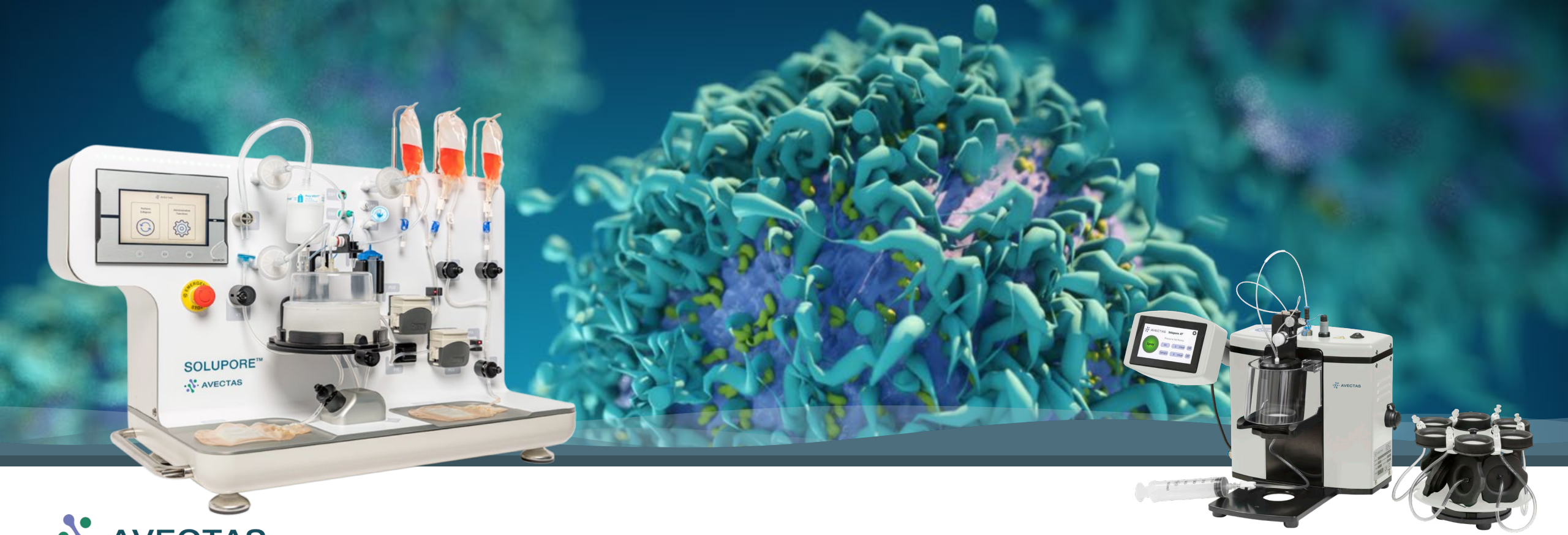

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SOLUPORE® – ENABLING THE NEXT WAVE OF CELL THERAPIES

Cellicon Valley '21 - The Future of Cell and Gene Therapies

Michael Maguire PhD, CEO, Avectas

NEW CELL ENGINEERING PLATFORM

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Current cell therapies:

KYMRIAH® (tisagenlecleucel) Suspension for IV infusion

TECARTUS™ (brexucabtagene autoleucel) Suspension for IV infusion

Current approved cell therapies have single modification

YESCARTA® (axicabtagene ciloleucel) Suspension for IV infusion

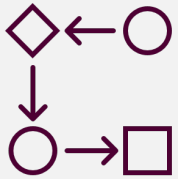
Breyanzi

Next-generation therapeutics require:

- Complex cell engineering capabilities, non-viral
- Compatibility with viral engineering
- Maintenance of cell viability and functionality

SOLUPORE technology enables:

1. Complex, multi step, sequential editing for next-gen autologous and allogeneic products

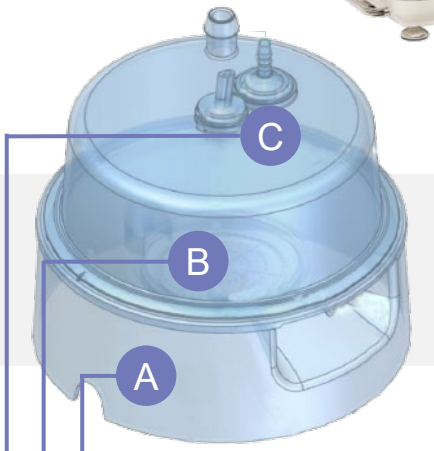


2. Transfection pre- and post-viral plus rationalization of various up/down stream unit process reducing time and steps

3. Clinical engineering of finite and fragile cell populations for autologous and allogeneic therapies while maintaining cell functionality

SOLUPORE WORKS IN FIVE SIMPLE STEPS

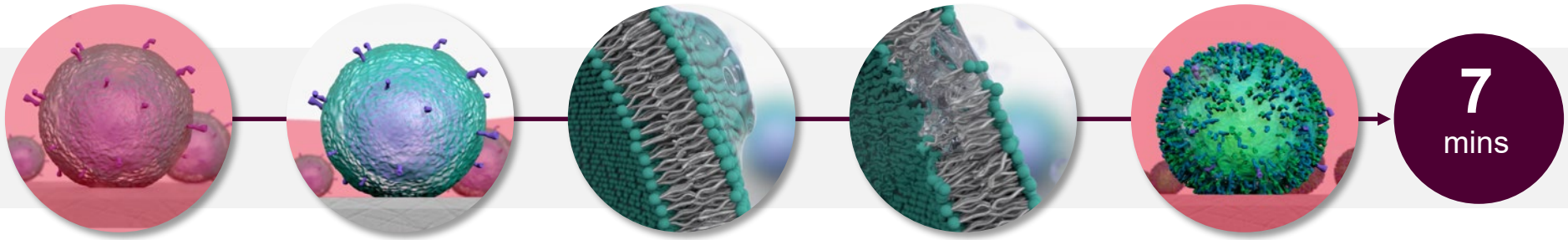
A gentler process to transfection brings multiple benefits including **high transfection efficiency and high viability**



C Precision atomiser for delivery

B Custom designed cell filter membrane

A Closed single-use transfection chamber



Cells transferred to single use chamber

Culture medium briefly removed

Cells precision sprayed with cargo-delivery solution

Cell membrane transiently permeabilised enabling cargo to pass through

Engineered cells resuspended in culture medium *(no washing step required)*

SOLUPORE SUS

Powerful, non-viral clinical-grade cell engineering system

Closed, GMP aligned Platform

- Gentle, clinical grade cell engineering
- V. low genomic perturbation of cells
- Potential to condense manufacturing process

Excels in complex editing for difficult to engineer cells

- Overcomes the limitations of electroporation and viral vectors
- Addresses Autologous and Allogeneic therapies

High Value Applications

- Gentle Modification of IPS cells
- Modification of Fragile and scarce cells e.g. TILs
- Post transduction editing of T and NK

Spans Research to Clinical Use

Easy, automated, rapid

- high viability and optimal efficacy of cells, post-process
- Technology spans research use to high-throughput applications

SOLUPORE RESEARCH TOOL

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Reproducible cell engineering system for discovery and feasibility studies

Tech transferrable

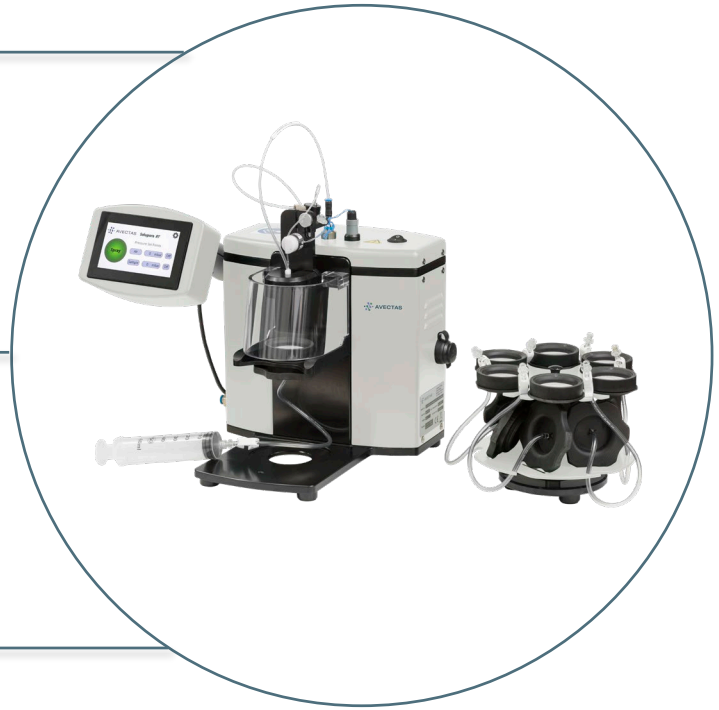
Ready for technology transfer.
Easy transfer into standard
R&D laboratory setting

Ease of Use

Rapid, simple process with
minimal steps.

Technical support and data

In place protocols and
comprehensive data set support
adoption through to of SOLUPORE



- Continuous system to increase process throughput and accelerate manufacture
- Allogeneic cell scale manufacture
- 1 x10^{9} –1 x10^{10}+ cells

REGULATORY PATHWAY FOR CORE ELEMENTS

Delivery Solution

Single Use Assembly

Multi Use Controller

SUS Regulatory: Avectas will file a Type II and Type V DMF and will provide supporting documentation

PATHWAY FROM CONCEPT TO COMMERCIALISATION

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Feasibility studies

SOLUPORE RT (Research Grade Tool)

- Scale: 10^6
- Evaluate technology under a co-developed program
- Research and collaboration agreement
- Tech transfer of SOLUPORE RT, consumables, protocols, supported by training and technical support.

Clinical grade system

SOLUPORE SUS cGMP ready

- Scale: 10^8
- Tech transfer of non-GMP and GMP system with technical and regulatory support from Avectas

Flow-through System

SOLUPORE FTS

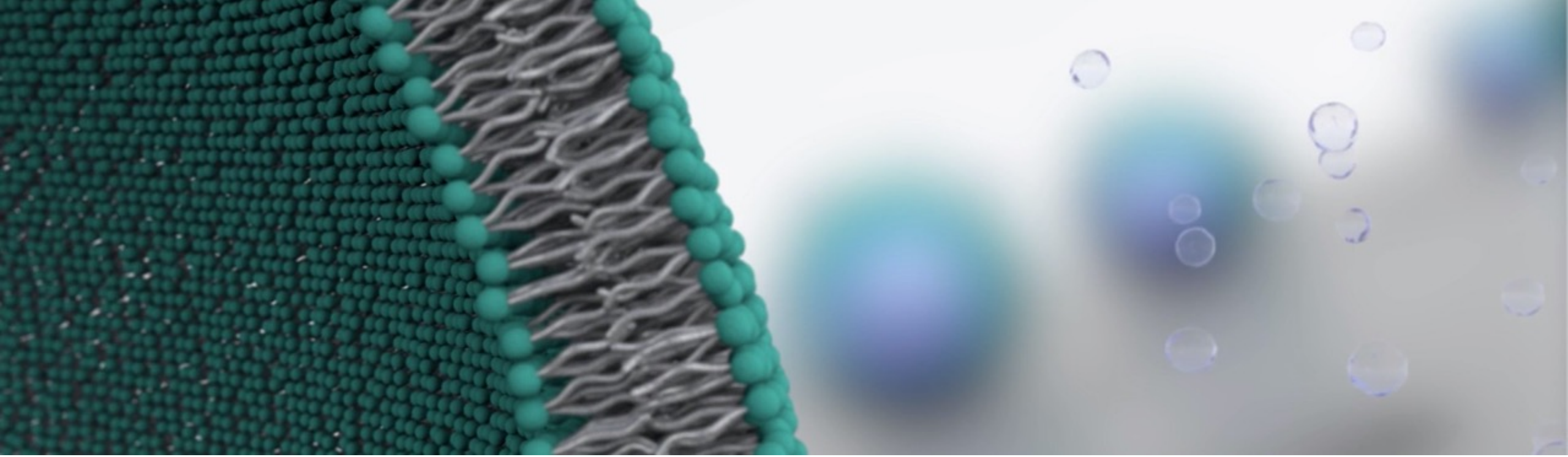
Flow through system
- In development

- Allogeneic cell scale manufacture

- 1×10^9 + cells

Commercialisation with partners

Commercialisation Agreements



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SOLUPORE PERFORMANCE DATA

SOLUPORE DELIVERY ACROSS A RANGE OF IMMUNE CELL TYPES AND GENE EDITING PLATFORMS

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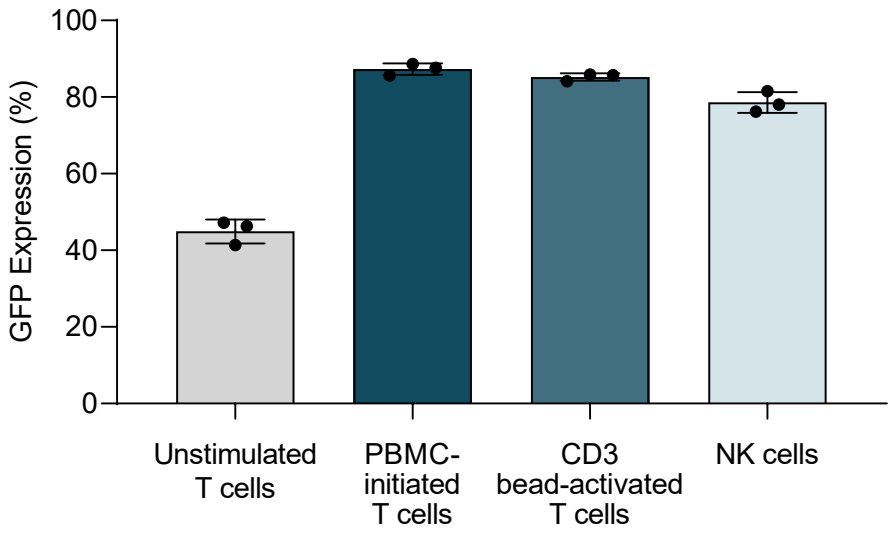
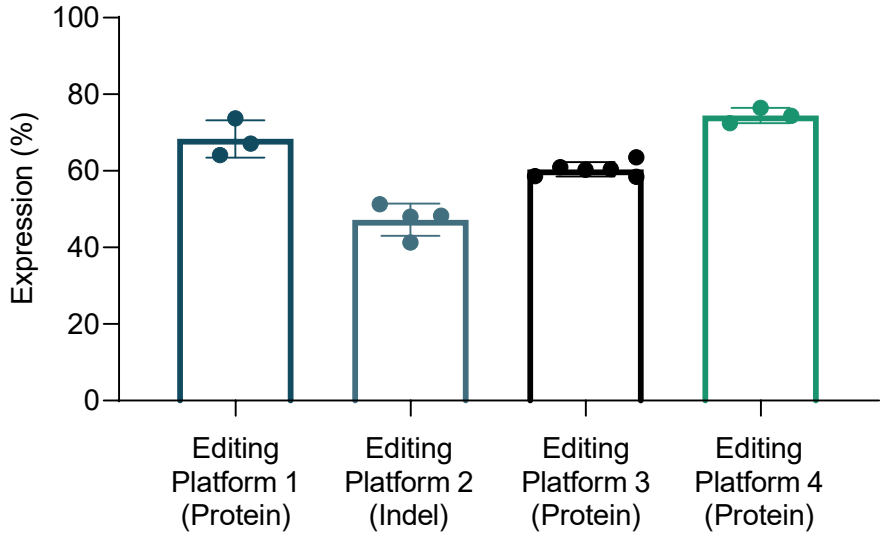
Multiple Immune Cell Types GFP mRNA



> 80 %
cell viability retained in all experiments

Multiple Gene Editing Platforms



Versatile platform, compatible with broad range of immune cell culture methods and gene editing platforms

SOLUPORE TECHNOLOGY SHOWS HIGH CRISPR RNP EDIT EFFICIENCY ACROSS A RANGE OF TARGETS IN IMMUNE CELLS

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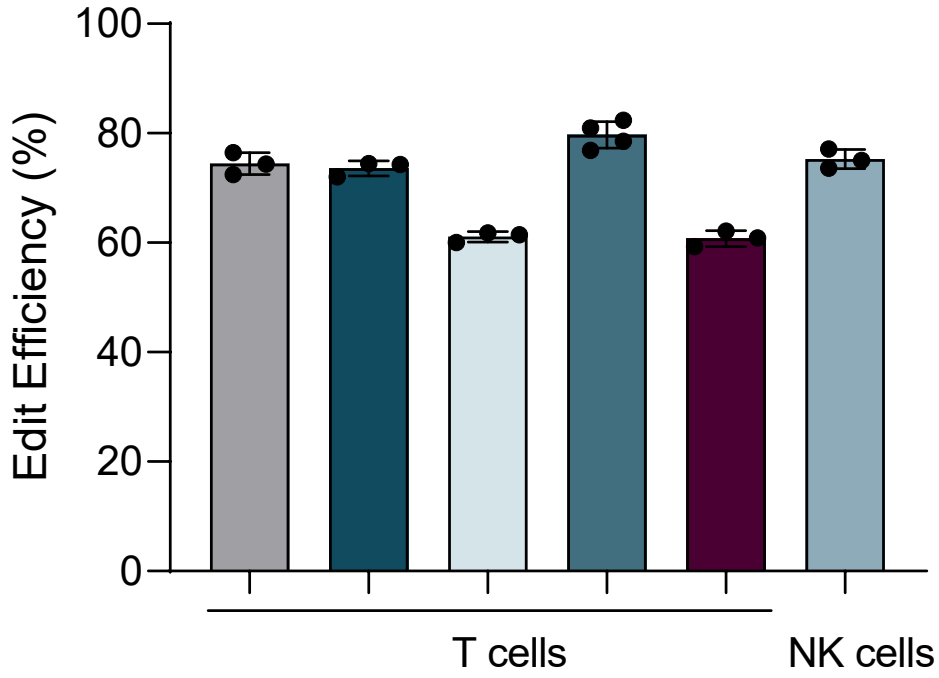
CRISPR Edited T and NK Cells



> 80 %
cell viability
retained in all experiments

SOLUPORE technology is compatible with CRISPR gene editing tools in both T and NK Cells

VIRAL TRANSDUCTION FOLLOWED BY SOLUPORE DELIVERY

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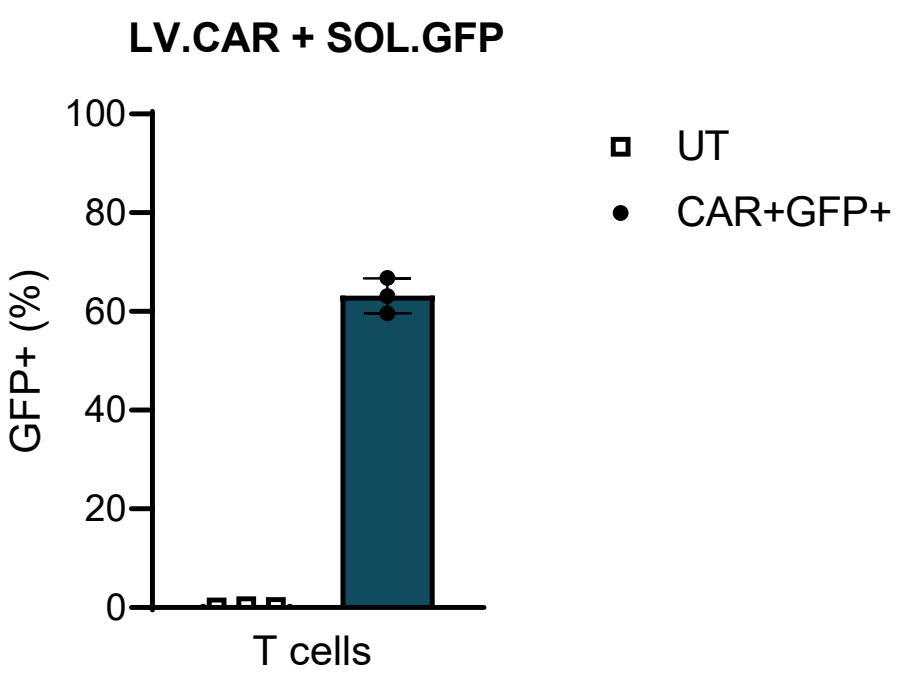
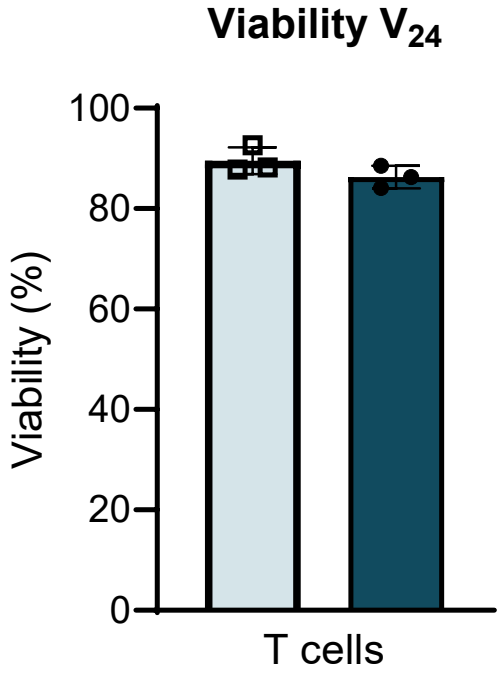
SOLUPORE transfection of LV transduced T cells

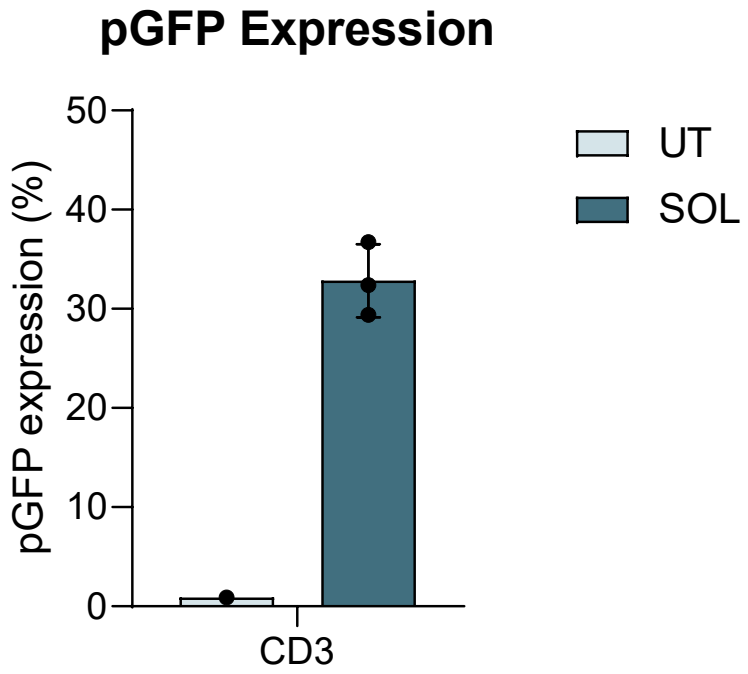


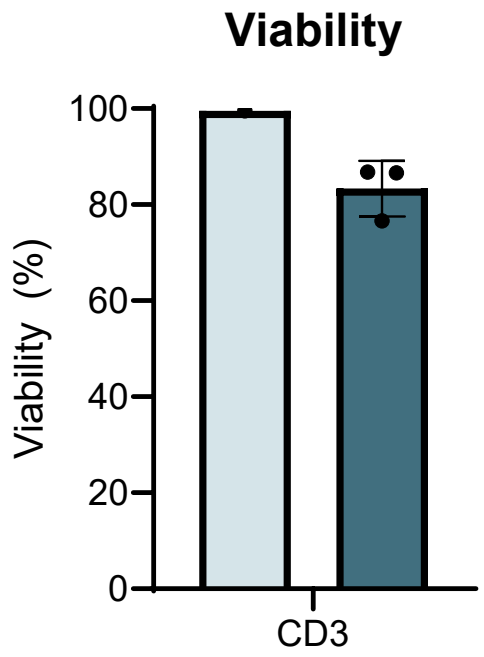


SOLUPORE technology supports next-generation engineering of virally transduced effector cells

SOLUPORE DELIVERY OF DNA

SOLUPORE delivery of plasmid GFP to T cells





Demonstrated reproducible delivery of plasmid GFP (5.7kb) to isolated CD3+ T cells

SOLUPORE TECHNOLOGY ENABLES COMPLEX CELL ENGINEERING WHILE MAINTAINING HIGH CELL VIABILITY

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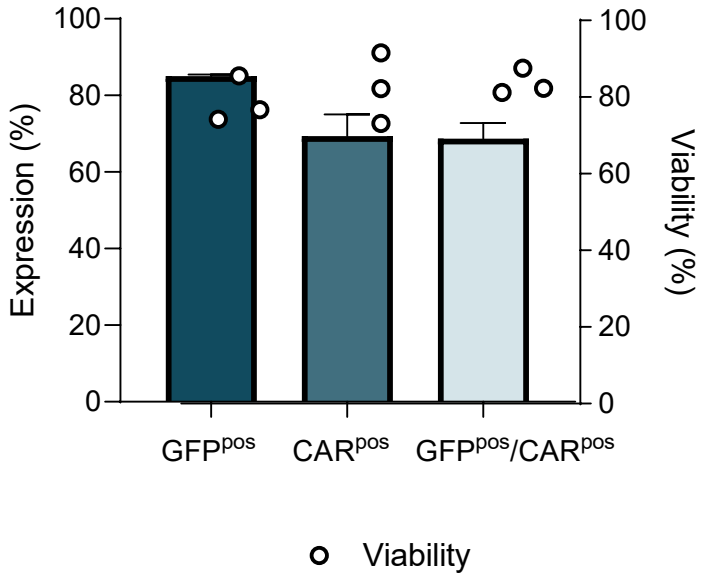
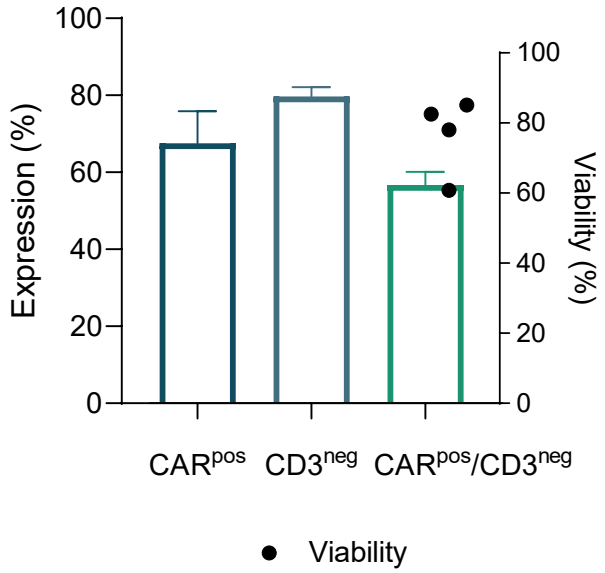
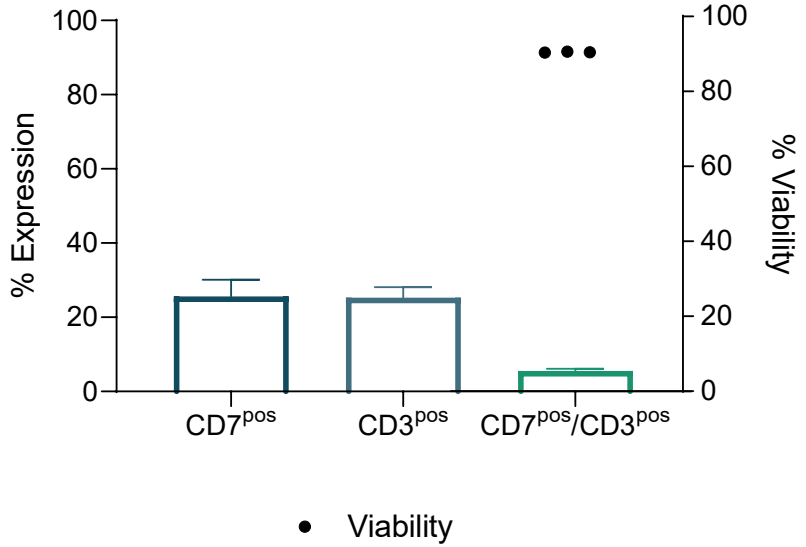
Multiplex Delivery
CD19 CAR & GFP mRNA



Sequential Delivery
Day 0: TRAC RNP
Day 2: CD19 CAR mRNA



Sequential Delivery
Day 0: TRAC RNP
Day 2: CD7 RNP



SOLUPORE technology supports complex engineering of next-generation effector cells

SOLUPORE DELIVERY PROCESS MINIMALLY PERTURBS IMMUNE GENE EXPRESSION IN T CELLS

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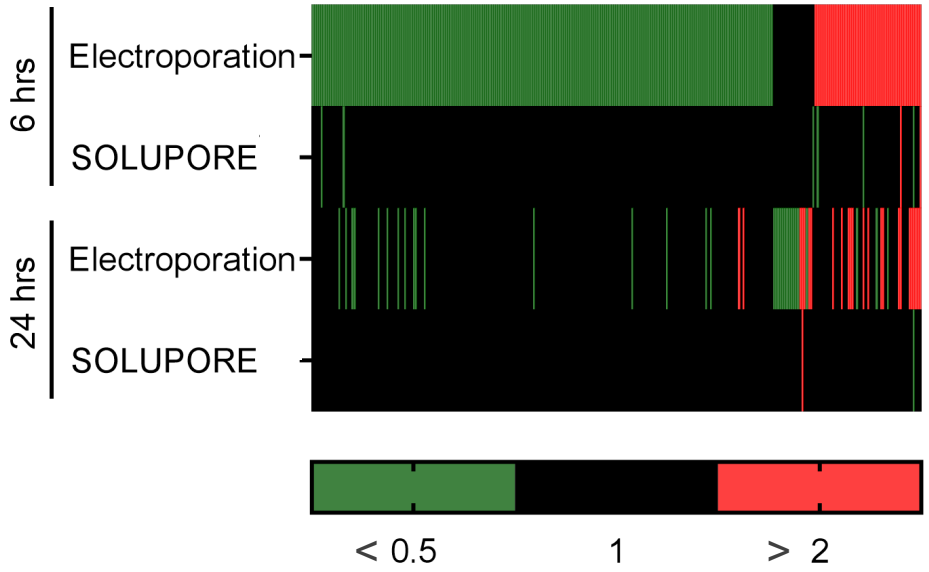
Minimal disruption of immune gene expression post-SOLUPORE

Mis-regulated immune genes post-treatment



Pathway (600 genes in panel)	SOLUPORE	Nucleofection
Activation (200)	4	77
Metabolism (193)	2	56
Exhaustion (103)	2	49
TCR signaling (48)	3	25
Apoptosis (48)	1	22
Chemokine signaling (22)	1	15
T cell migration and persistence (24)	0	11
Glycolysis (19)	0	8
Antigen processing and presentation (27)	0	6

Low-stress delivery method is desirable for preservation of effector cell functionality *in vivo*

SOLUPORE DELIVERY PROCESS MAINTAINS T CELL FUNCTIONALITY

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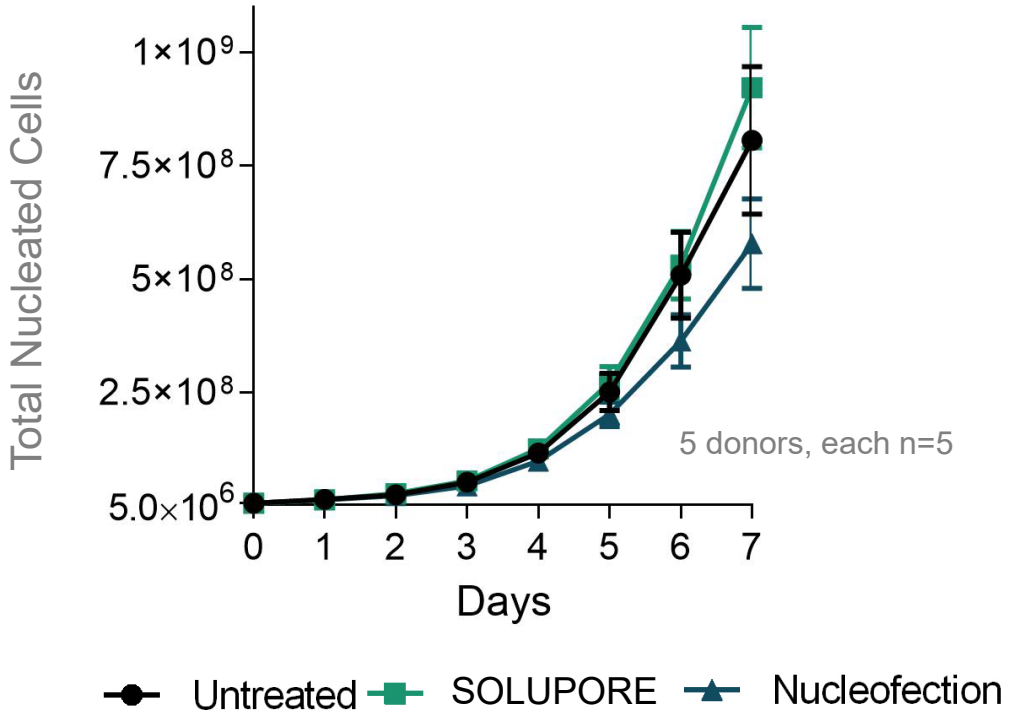
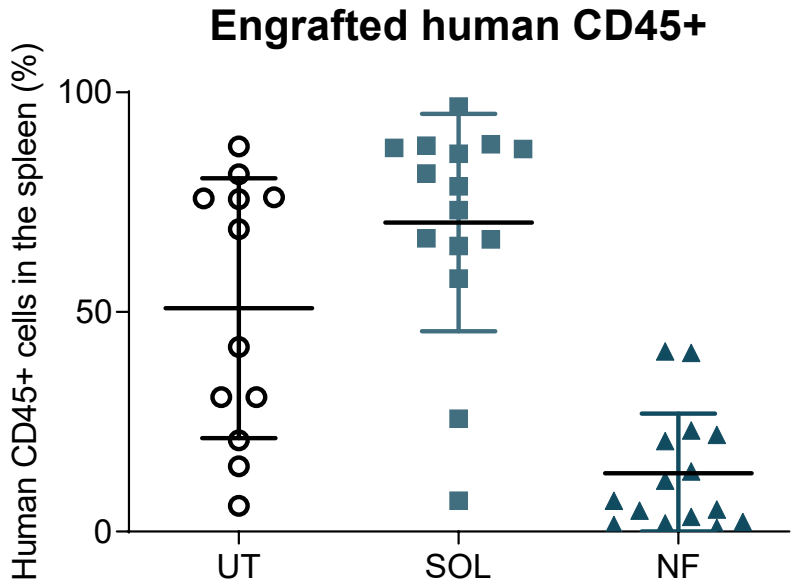
Maintained proliferative capacity in T cells post-SOLUPORE



T cells post-SOLUPORE successfully engraft in murine model



T cells maintain proliferative and engraftment functionality post-SOLUPORE process

SOLUPORE CAR-T CELLS ARE HIGHLY FUNCTIONAL *IN VITRO* AND *IN VIVO*

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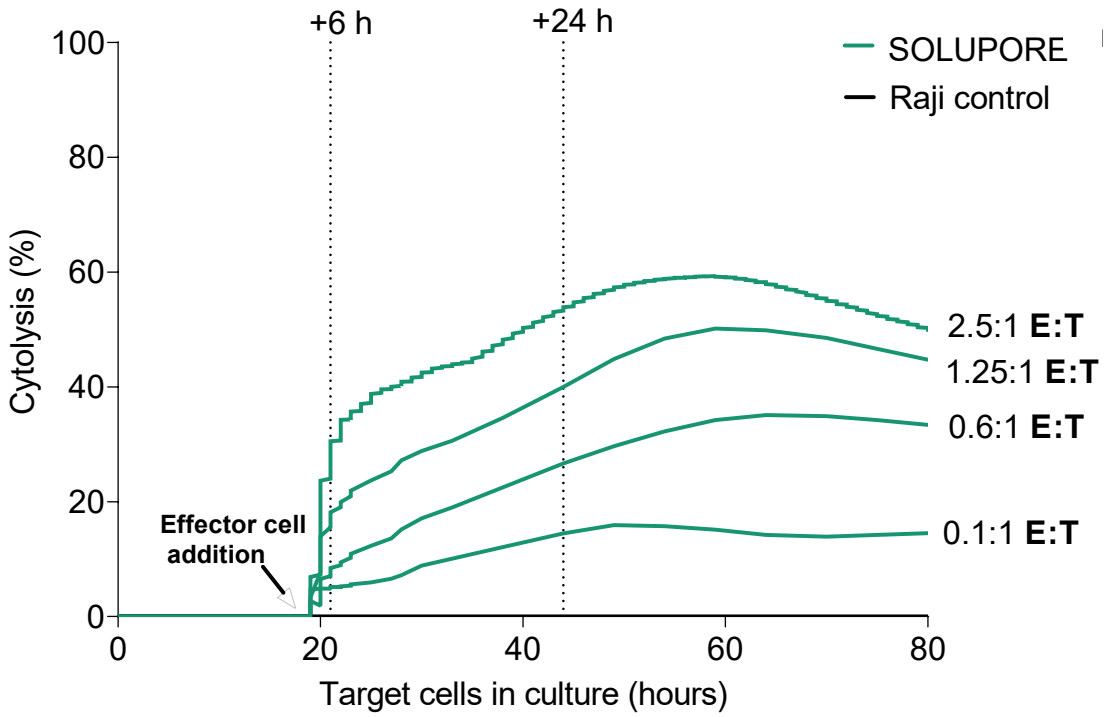
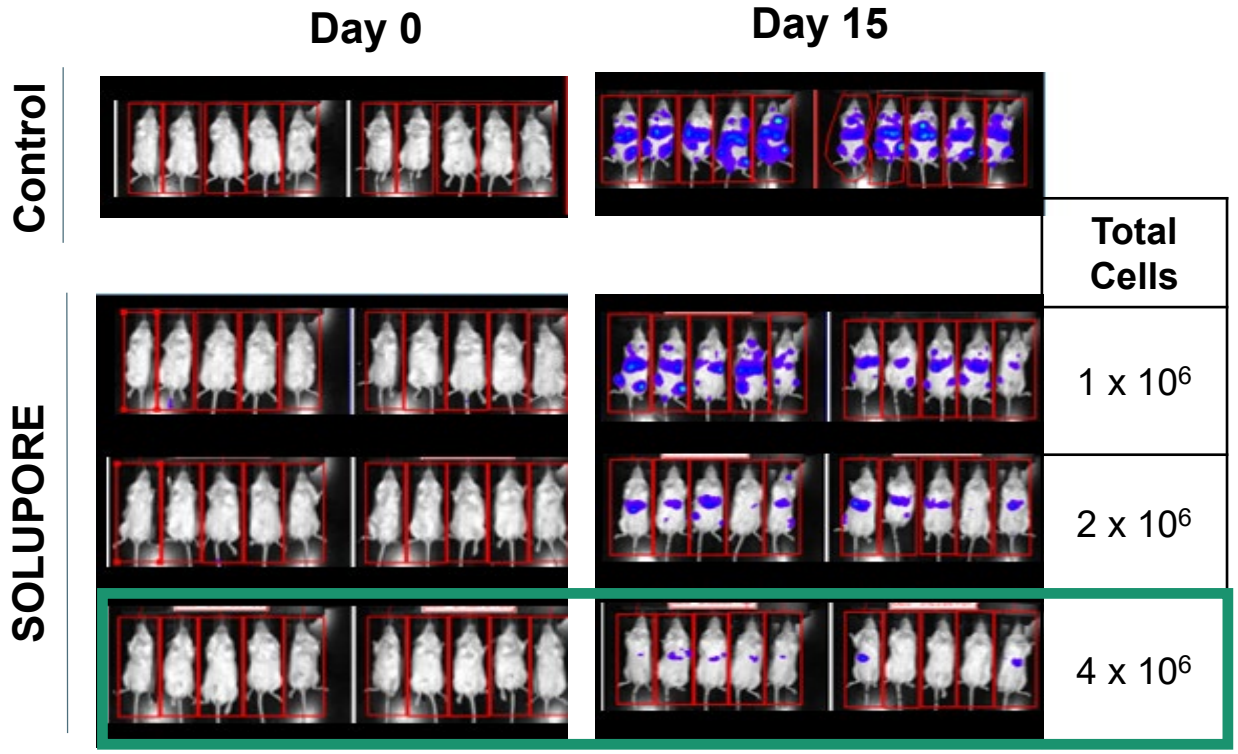
In vitro

Cell Killing Assay on xCELLigence System



In vivo



Evidence of disease-free mice at highest CAR-T cell dose demonstrates effector cell functionality *in vivo*

NEW AUTOMATED CELL ENGINEERING PLATFORM TO CLINICALLY MANUFACTURE NEXT-GENERATION CELL THERAPEUTICS

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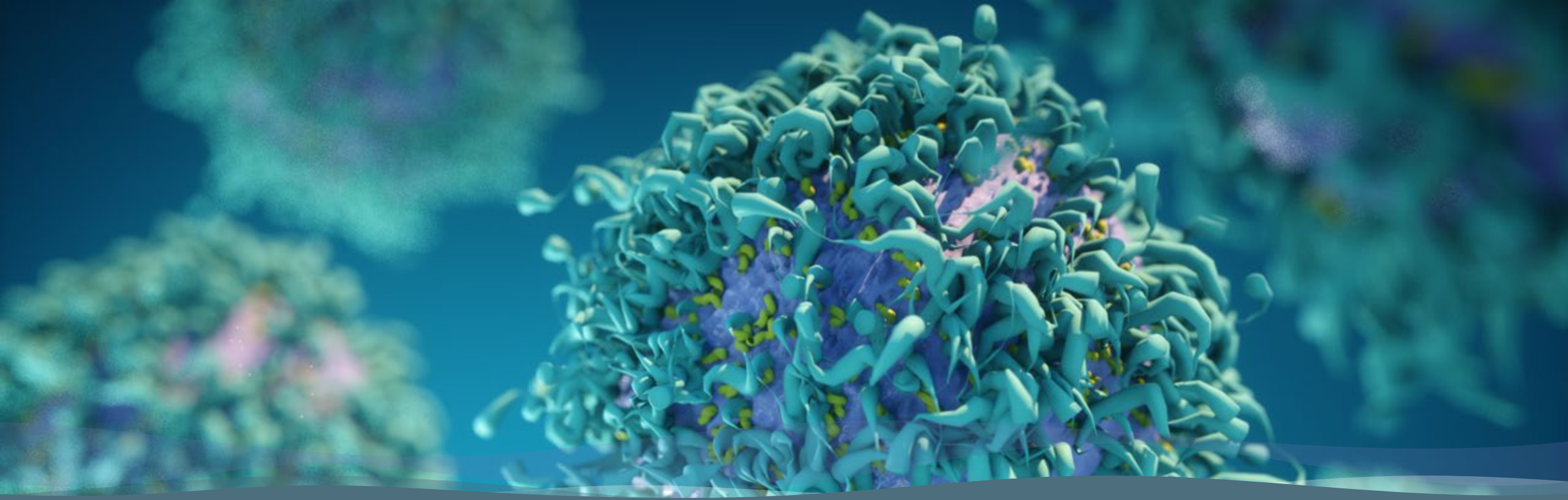
- SOLUPORE technology is **well tolerated** by cells; **increased efficacy** and **higher proliferation** post processing
- For autologous therapies, enables **delivery to fragile cell** populations (T-cells, NK cells) and involving pre/post transduction edits
- Enables **multiplexing** and/or **sequential editing** for allogeneic and solid-mass tumour cell therapy
- Delivery of **variety of cargos**
- Research device available now, Clinically aligned device available Q2 2021
- Anticipated **DMF filings** by end of 2021



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THANK YOU

Contact: Michael Maguire
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mmaguire@avectas.com