

# Push a Button and Walk Away Cell Therapy Manufacturing

 *trenchant*

# The AutoCell Mission

## key driving principles

# “Cell Therapy Proximity”



# The AutoCell proximity solution

**Cost:** Reduce COGS of CGT

**Access:** Reduce “vein” to “vein” time from 4-6 weeks to 2.5 days

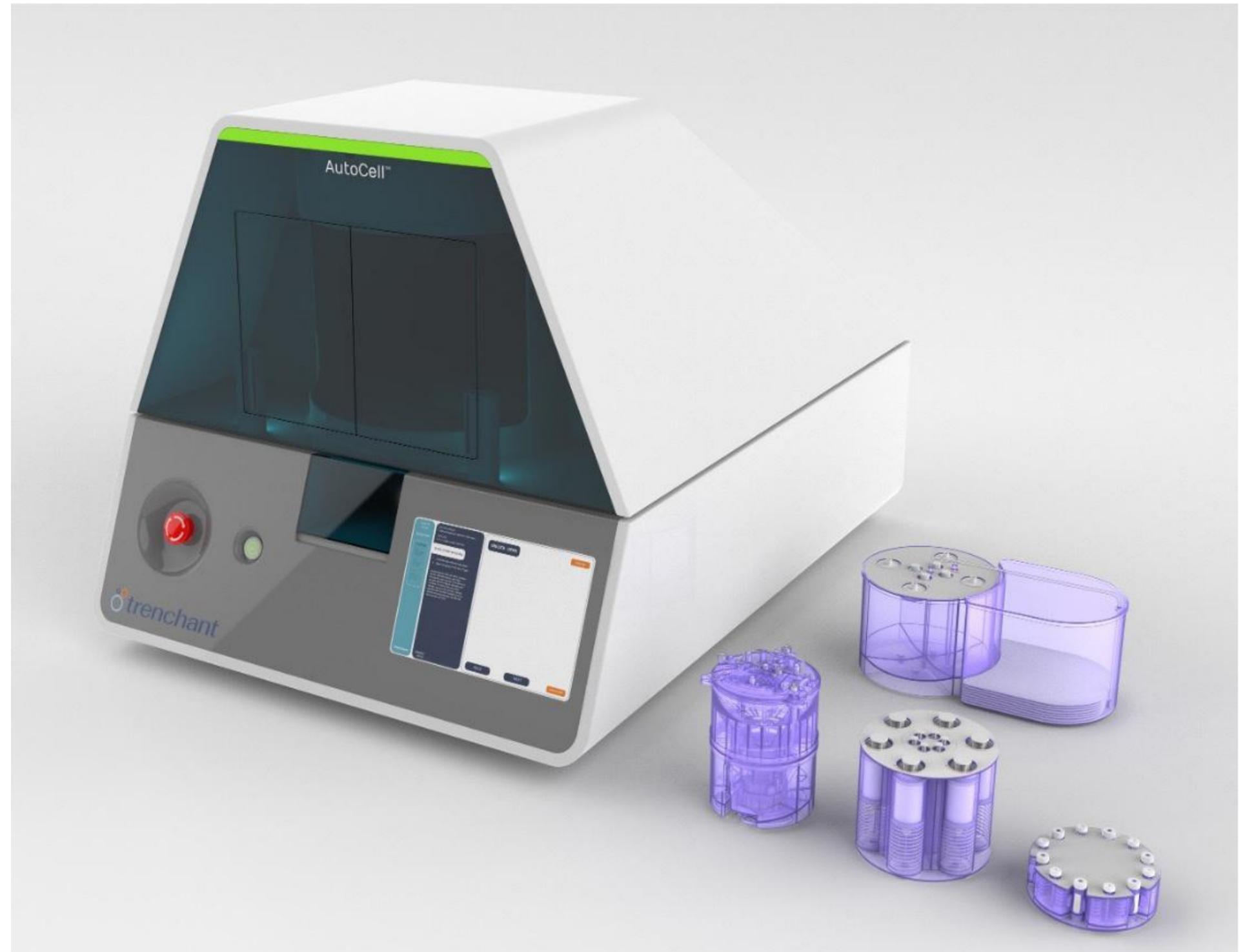
**Efficiency:** Increases manufacturing efficiency from 7.9% to 65.0%. (823%)

No-ex-vivo expansion

**Sustainability:** A 5x to 20x reduction in plastic

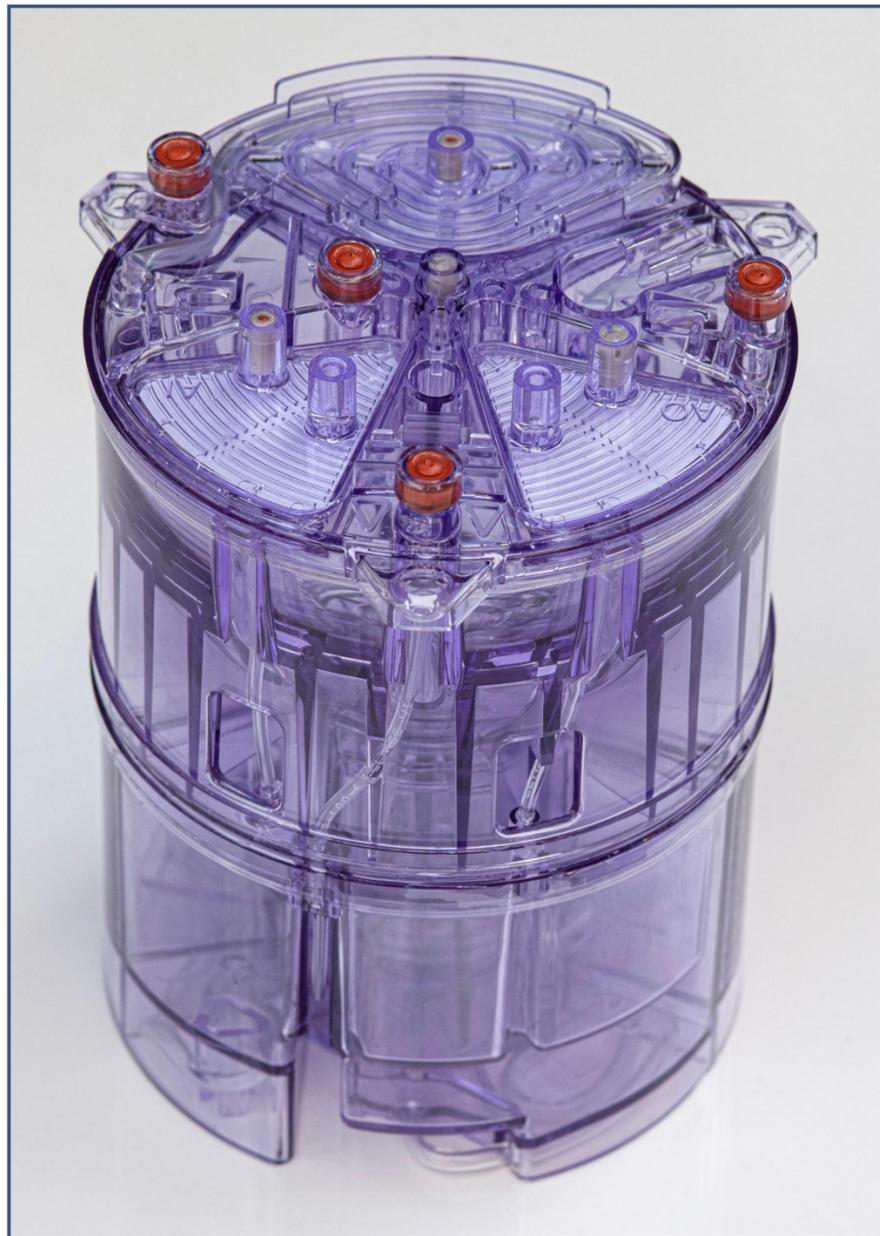
**Safety:** Only one cell transfer.  
A lower risk to cells & operators

**Quality control:** Integrated analytics in a digital batch record for quality release

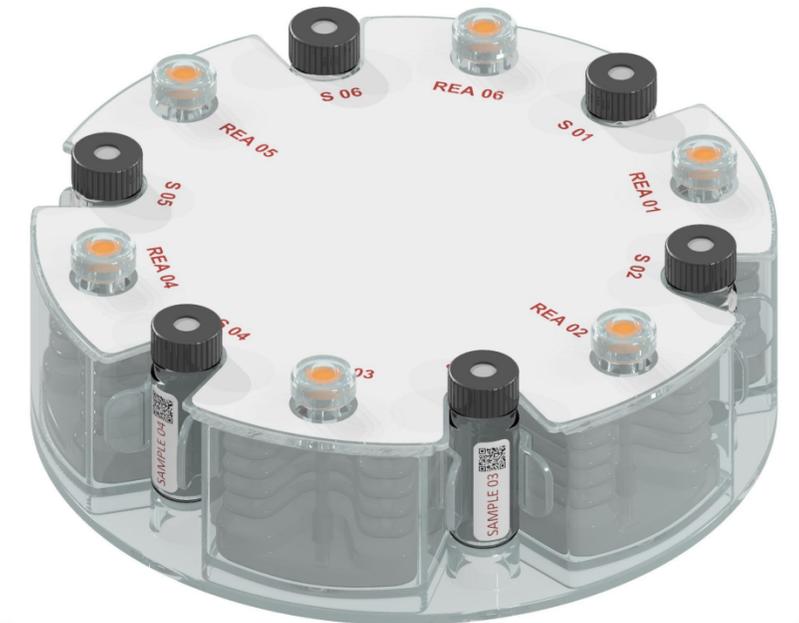
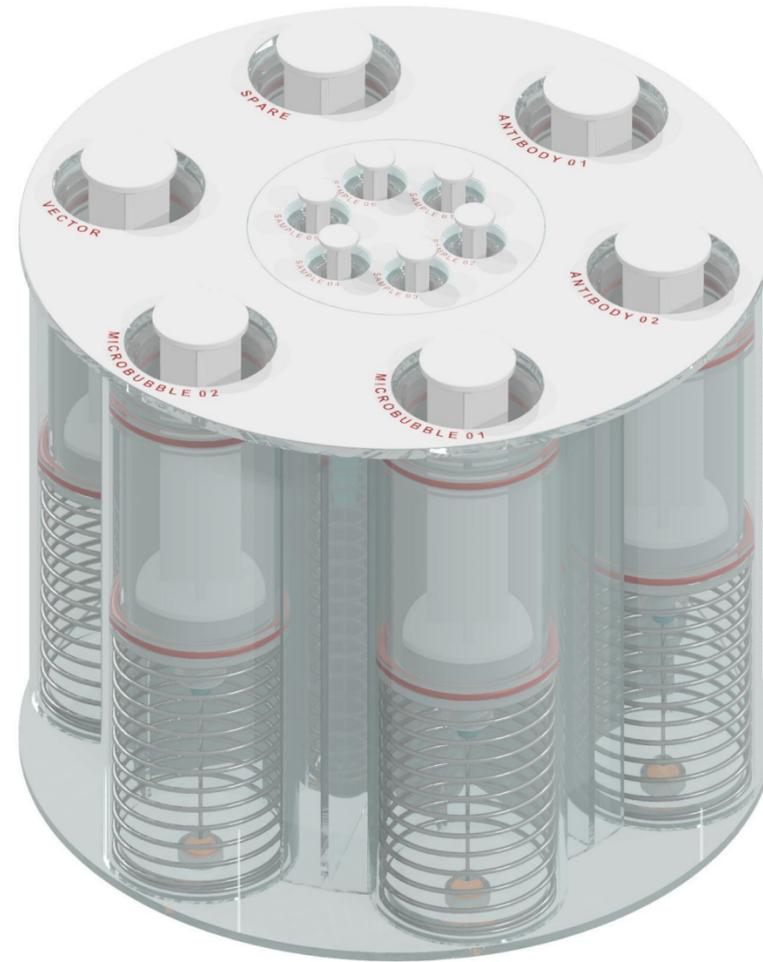
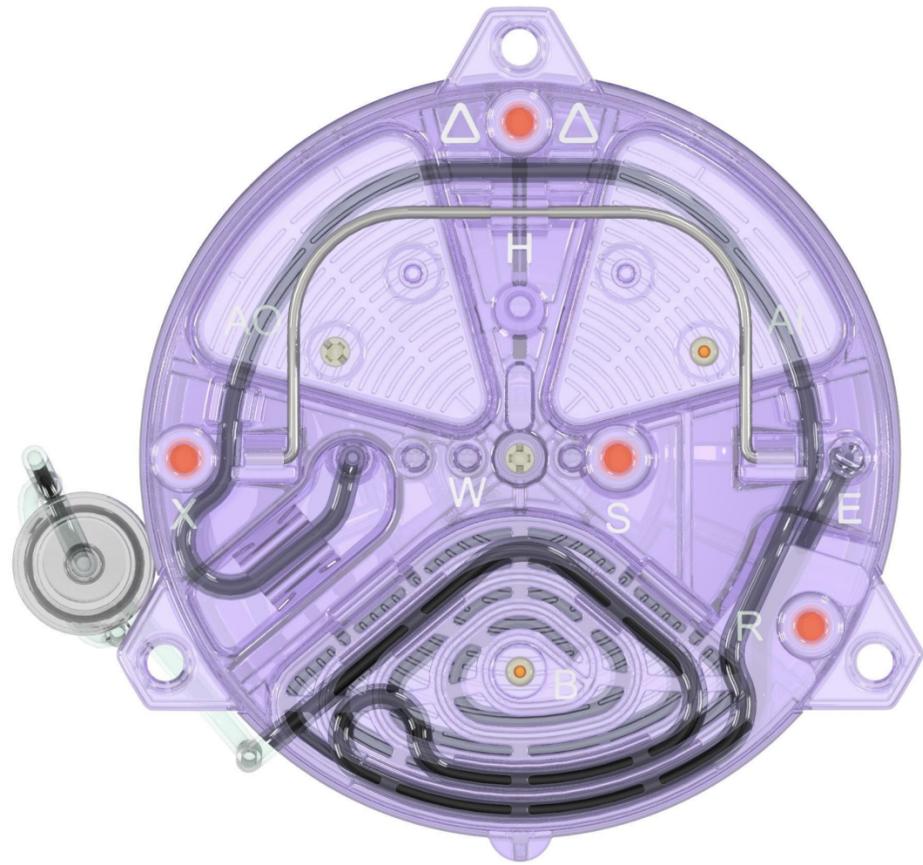


# AutoCell's Cell Processing Cassette (CPC)

Patient's cells go in, gene-modified cells come out



# AutoCell's Aseptic transfers of reagents and cell suspension samples





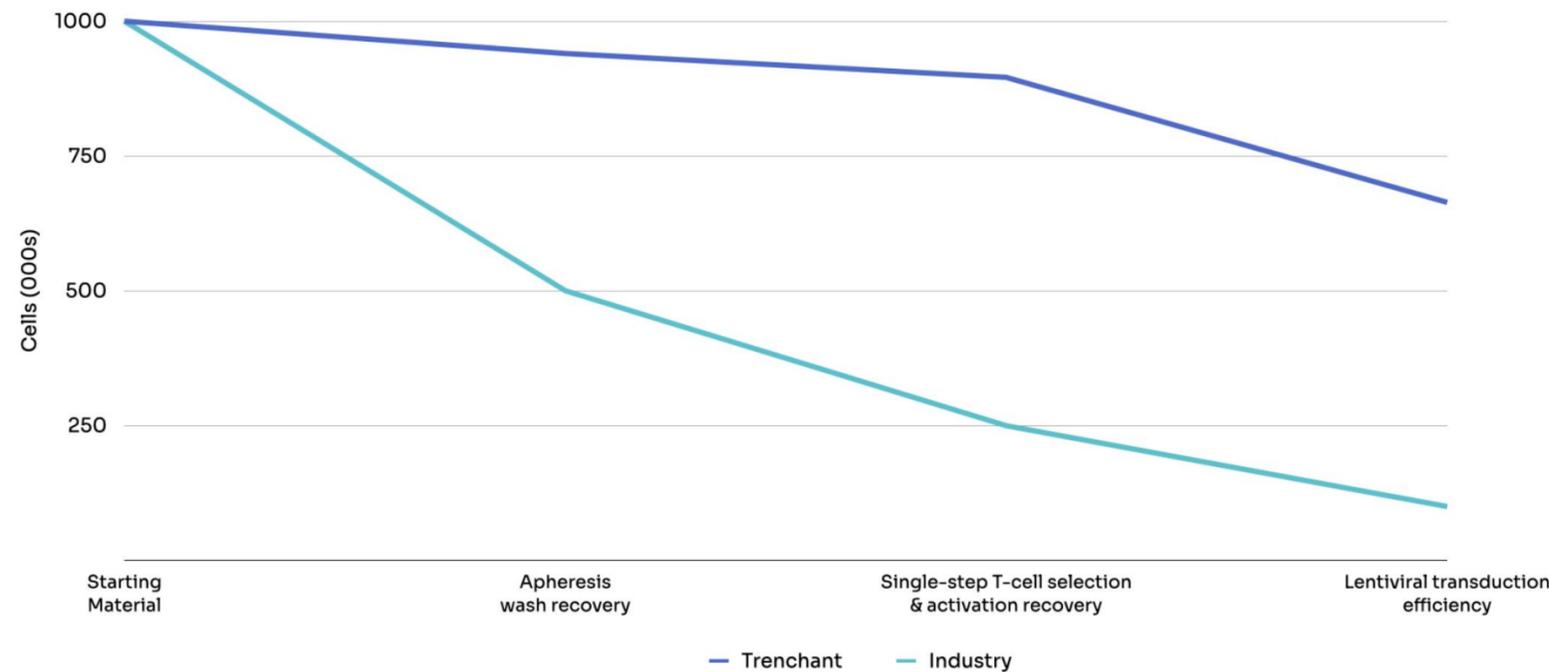
# SECTION 2

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How superior is the AutoCell processing performance over legacy systems?

# Semi-automated Alpha Prototype allows a lab technician to manufacture CAR-T cells in 25 days

Trenchant vs Industry Leader Cell Yield



	Leukapheresis Washing	Cell Selection & Activation	Transduction	Harvest Wash & Formulation	Cumulative Efficiency
Industry	50% <sup>1</sup>	49.9% <sup>1</sup>	39.4% <sup>1</sup>	80% <sup>2</sup>	<b>7.9%</b>
AutoCell	97.2% <sup>3</sup>	95.3% <sup>3</sup>	74.1% <sup>3</sup>	94.7% <sup>3</sup>	<b>65%</b>

<sup>1</sup> Francis, N. (2023). Development of an automated manufacturing process for large-scale production of autologous T cell therapies. *Mol Ther Methods Clin Dev* 16:31:101114 doi: 10.1016/j.omtm.2023.101114.eCollection 2023 Dec 14. <sup>2</sup> Personal Correspondence. <sup>3</sup> internal Report TRE\_LAB\_027



# SECTION 3

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What Makes AutoCell Superior to Existing legacy systems?

Our Cell selection and purification technologies

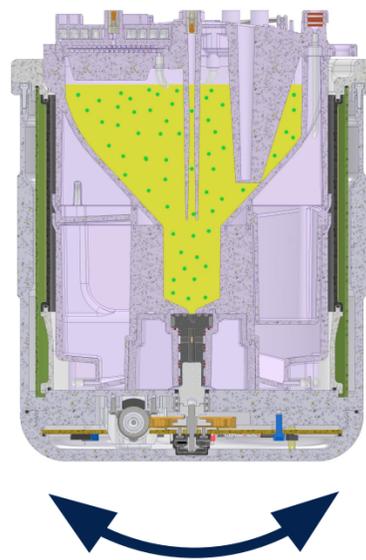
# Microbubbles select, activate & disengage simply & effectively



# AutoCell's Microbubble cell selection and activation is fast & simple.

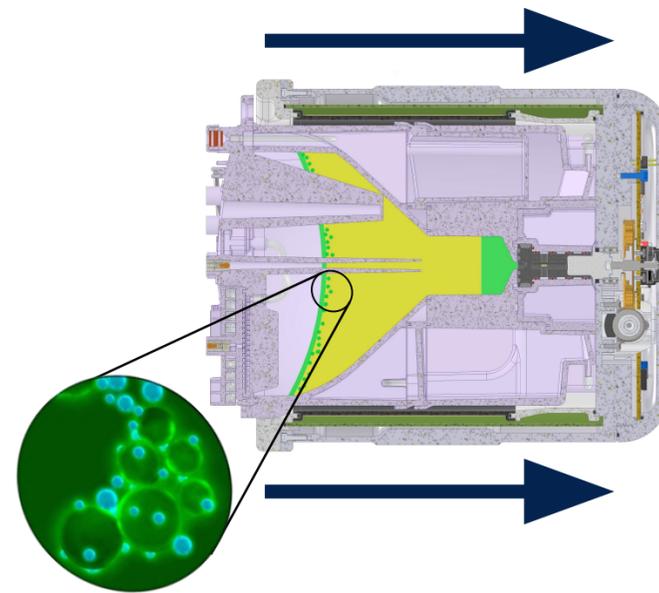
~95% recovery and 99% purity

**Step 1**  
Mixing & Incubation



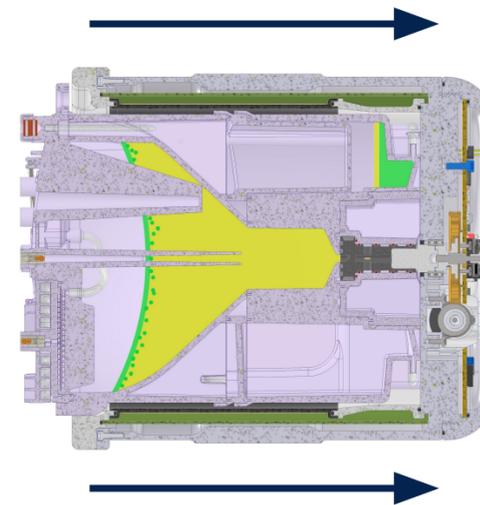
Incubate.  
T-Cells link to  
Microbubbles

**Step 2**  
Separation



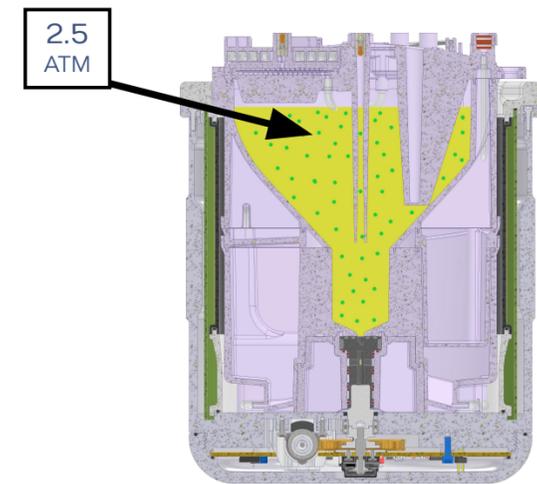
Centrifuge at 250 x G.  
Buoyant T-Cells  
separate from sedimenting,  
non-target cells

**Step 3**  
Non-target Cell Removal



Centrifuge at 50 x G.  
Transfer non-target cells  
Into depletion Chamber

**Step 4**  
MB De-Gas



Apply 2.5 ATM to collapse  
microbubbles.  
T-Cells return to normal buoyancy  
and begin activation

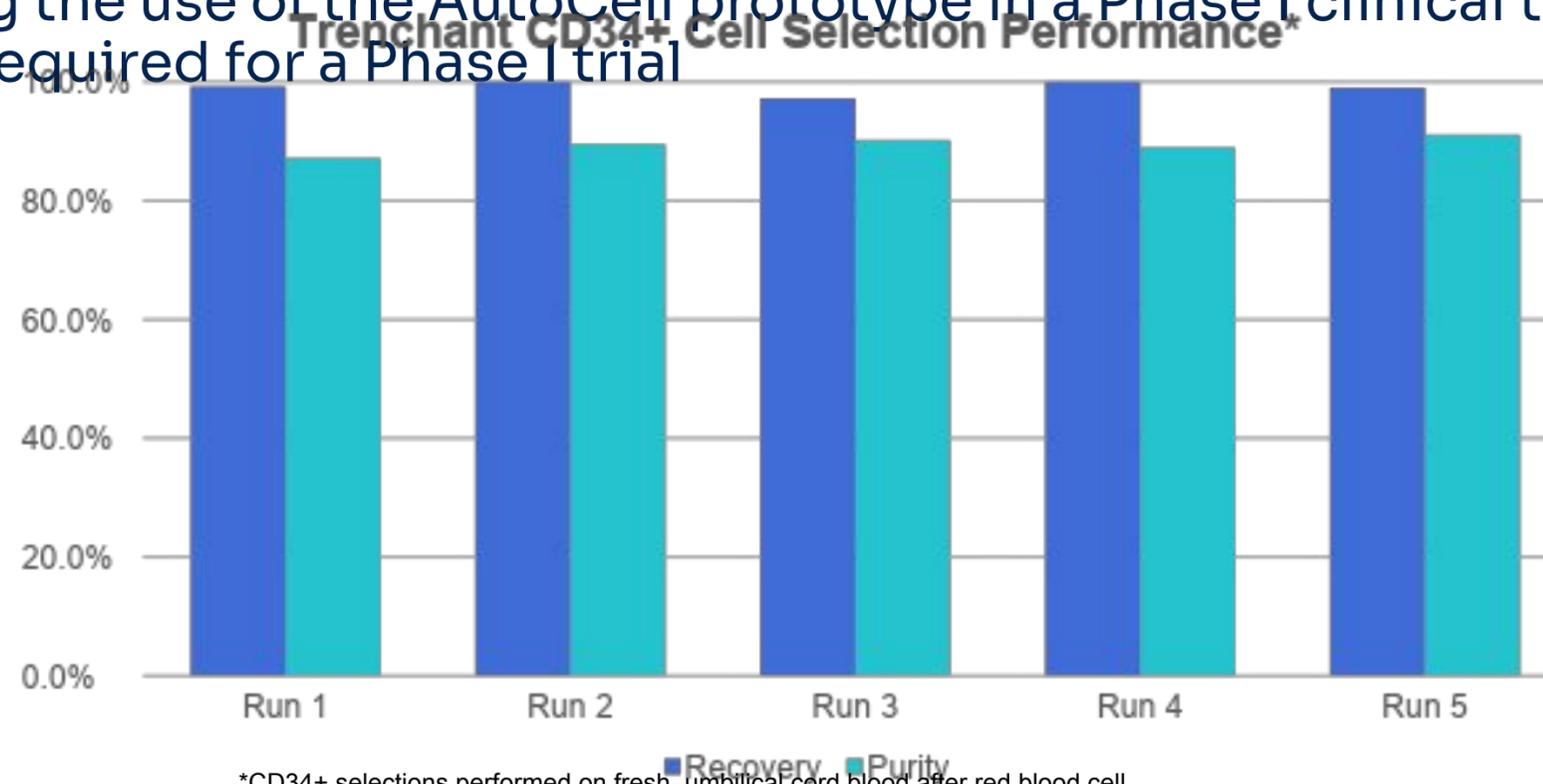
# Exploring other cell selection targets

## CD34+ for gene-modified HSC

Gene-modified CD34+ cells can be highly effective for the treatment of hemoglobinopathies, metabolic and genetic diseases.

AutoCell Cell Selection platform achieves superior recovery performance is significantly superior to the current market leader

We are currently discussing the use of the AutoCell prototype in a Phase I clinical trial for gene-modified CD34+ cells. "GMP" is not required for a Phase I trial



\*CD34+ selections performed on fresh, umbilical cord blood after red blood cell depletion

# AutoCell MBCSA technology enables sequential cell selection

Current, approved CAR-T therapies have limited control over T cell composition

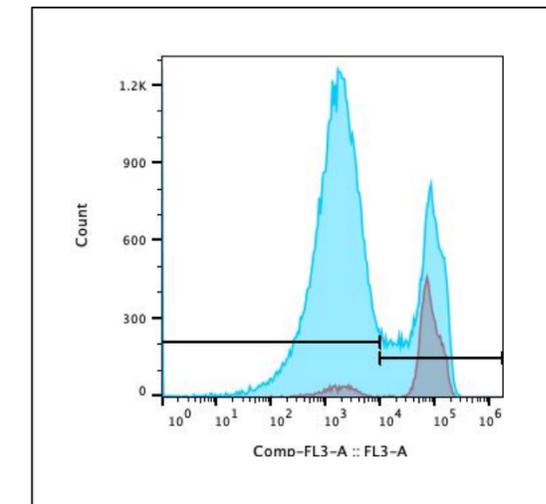
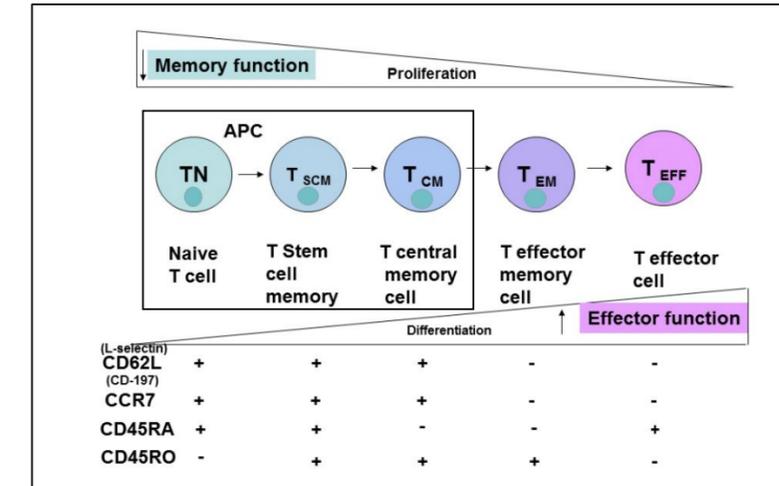
- Cytokine choice and concentration, culture medium composition and duration of expansion can impact T cell subsets, but considerable heterogeneity exists.
- Clinical data supports memory T cells as having a key role in the clinical outcome of CAR-T therapies\*
- Effector cells are good at killing tumor cells but get exhausted easily and do not persist in the body
- The ratio of CD4+ and CD8+ T cells has also been demonstrated to impact clinical outcome#

## Current Technology Limitations

- Existing, bead based, selection technologies cannot perform sequential cell selections as once T cells have been selected, they all have magnetic beads preventing further, magnetic discrimination
- Flow sorters are capable of multi-parametric sorting with high purity but do not have the throughput to be clinically useful

## MBCS Enables Sequential Cell Selection

- The unique properties of the MBCSA process enables de-gassing of the initial selection reagent and subsequent selection of a cell sub-population using a secondary reagent to create a more tightly refined and durable therapeutic agent



Initial studies demonstrated successful enrichment of CD8+ T cells from a pan T cell population

# AutoCell's Aptamer Linkers are superior to its competitors' antibodies

When optimization is completed, Trenchant will be able to provide AutoCell customers proprietary GMP-grade linkers for cell selection/activation at lower prices than currently available.

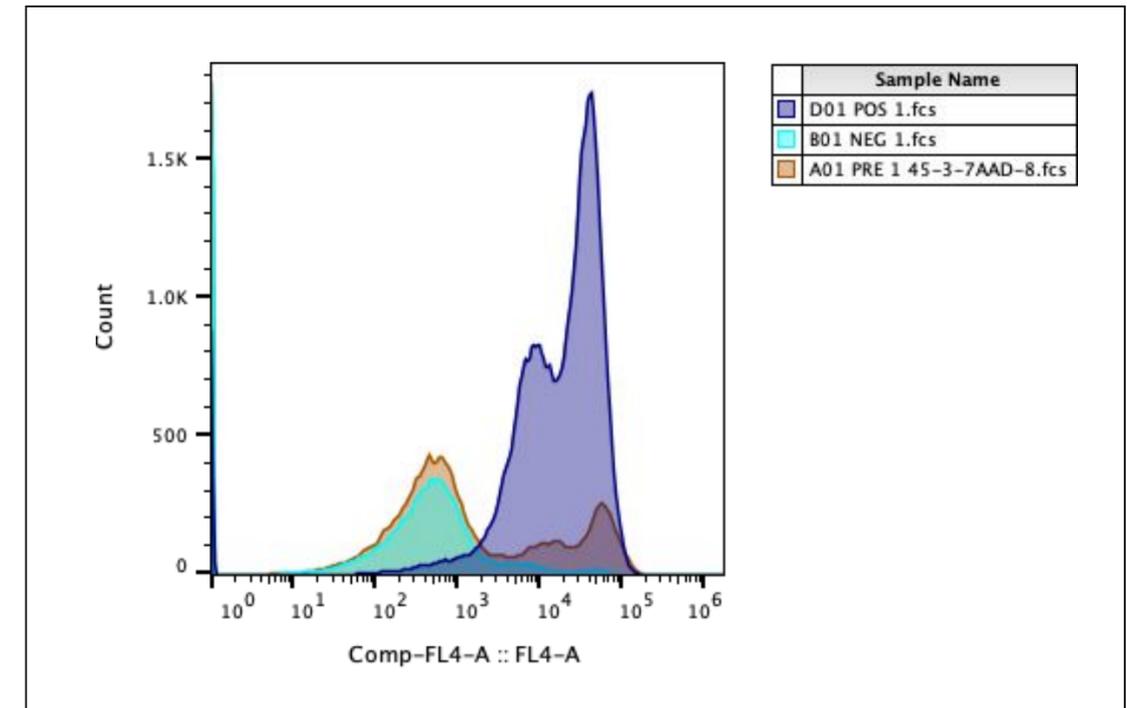
Aptamers are attractive alternatives to antibodies for MBCSA

- Aptamer price is ~ 1/10th of antibodies
- Faster pathway to GMP for new targets
- Customizable for specific clients
- Enable traceless selection

Trenchant has optimized aptamer performance and achieved similar performance to antibody-based selection

- Optimization of aptamer folding buffers and temperature profiles have ensured high specificity of aptamers for cell target (CD8)
- Low shear MBCS process is not impacted by lower affinity of aptamers to target than antibodies

CD8 Aptamer Selection Performance



	CD8+ Purity	CD8+ Recovery
Pre	16.5%	N/A
Negative Fraction	2.8 %	12.0%
<b>Positive Fraction</b>	<b>95.1%</b>	<b>89.1 %</b>



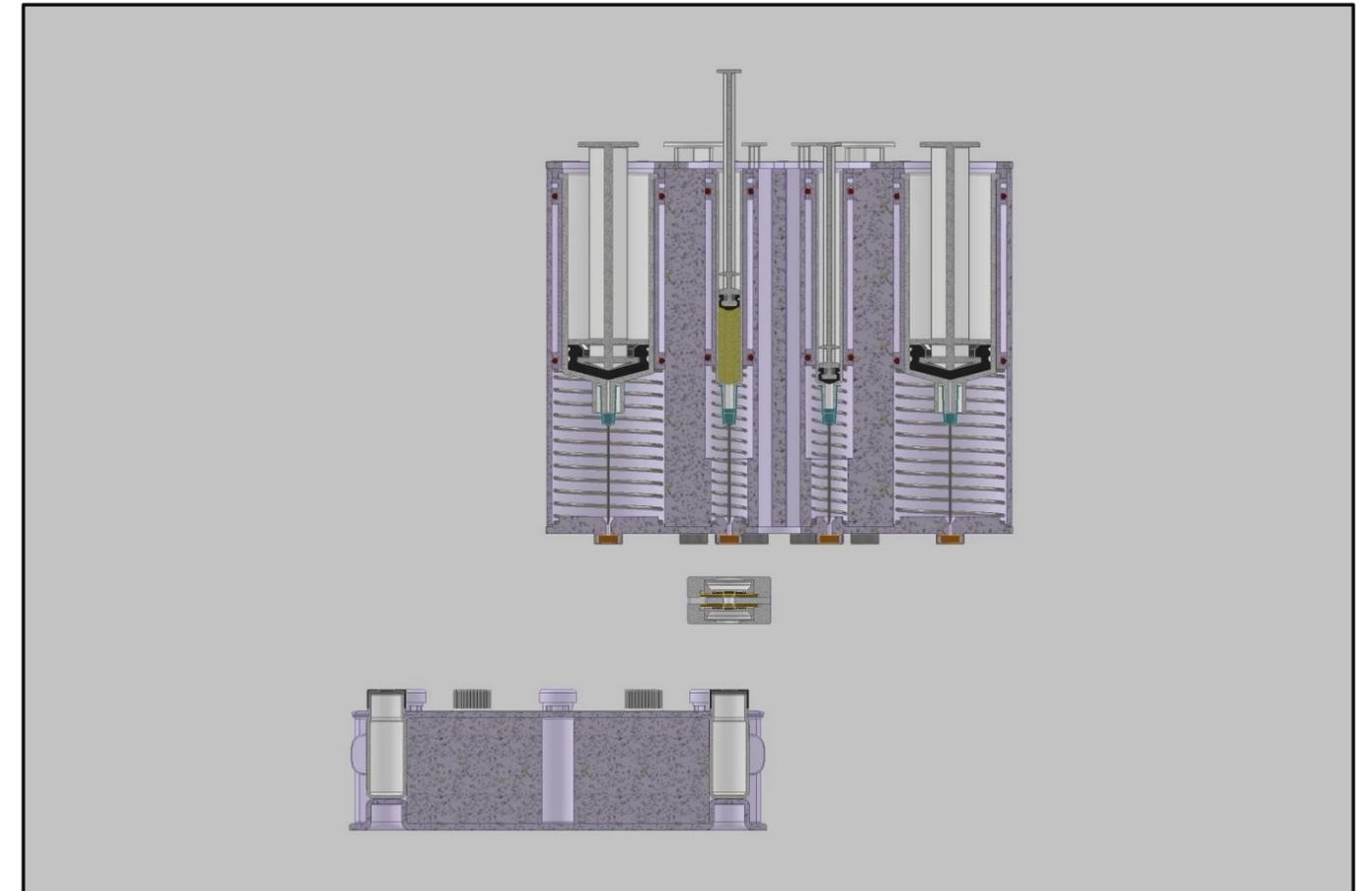
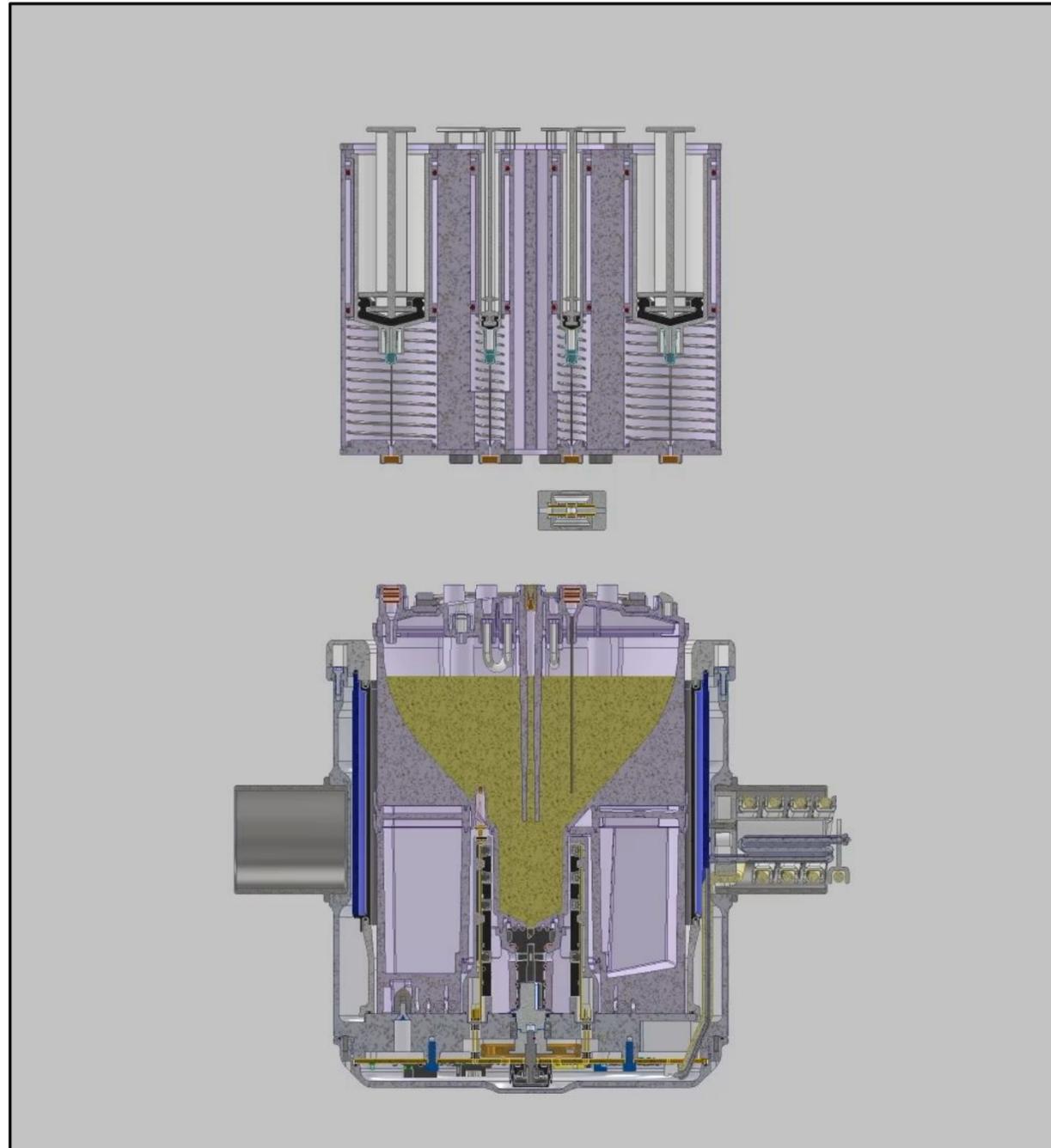
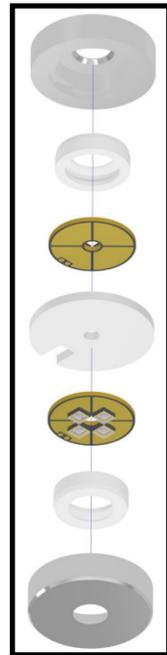
# SECTION 4

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Our Aseptic Transfer Technologies & the  
Single Cell Processing Cassette (CPC)

# Aseptic cell suspension sampling and integrated analytics

6 log UV disinfection (*Aspergillus brasiliensis*) of opposing septa in < 5 sec.



# Our Prototype Platform Has Been Tested In Collaboration With Invetech

	Leukapheresis Washing	Cell Selection & Activation Recovery	Cell Selection & Activation Purity	Transduction
Internal Data	97.2%	95.3%	98.8%	74.1%
Third Party Data	94.3%	96.4%	98.4%	74.6%





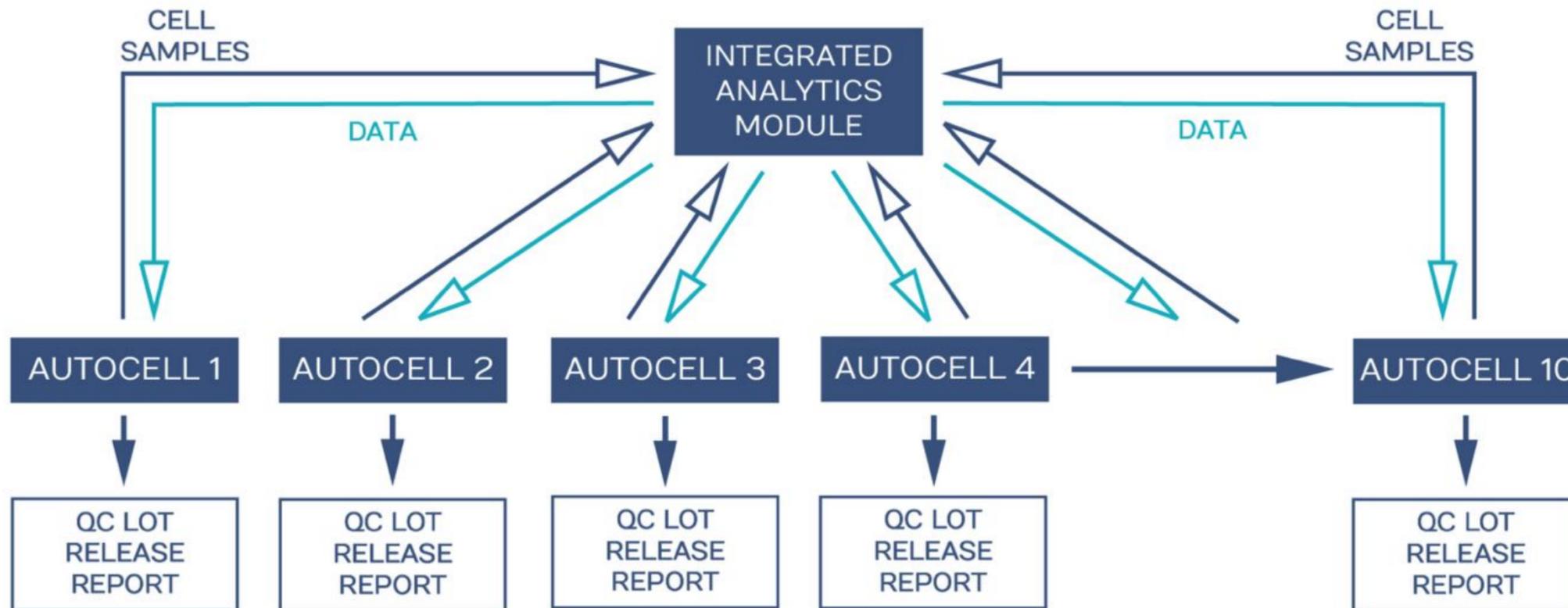
# SECTION 5

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Our Integrated Analytics Technologies

# Trenchant has partnered with a global leader To automate and integrate analytics

A partnership will be announced soon



## Integrated Analytics QC Tests

- Sterility
- Endotoxin
- Mycoplasma
- Residual virus
- Quantity CAR+ Cells & Purity
- Viability
- Vector Copy Number
- Identity
- Potency