



# Applying 20 Years of Cell Therapy Point-of-Care Manufacturing Lessons to Automated CD19 CAR-T Production

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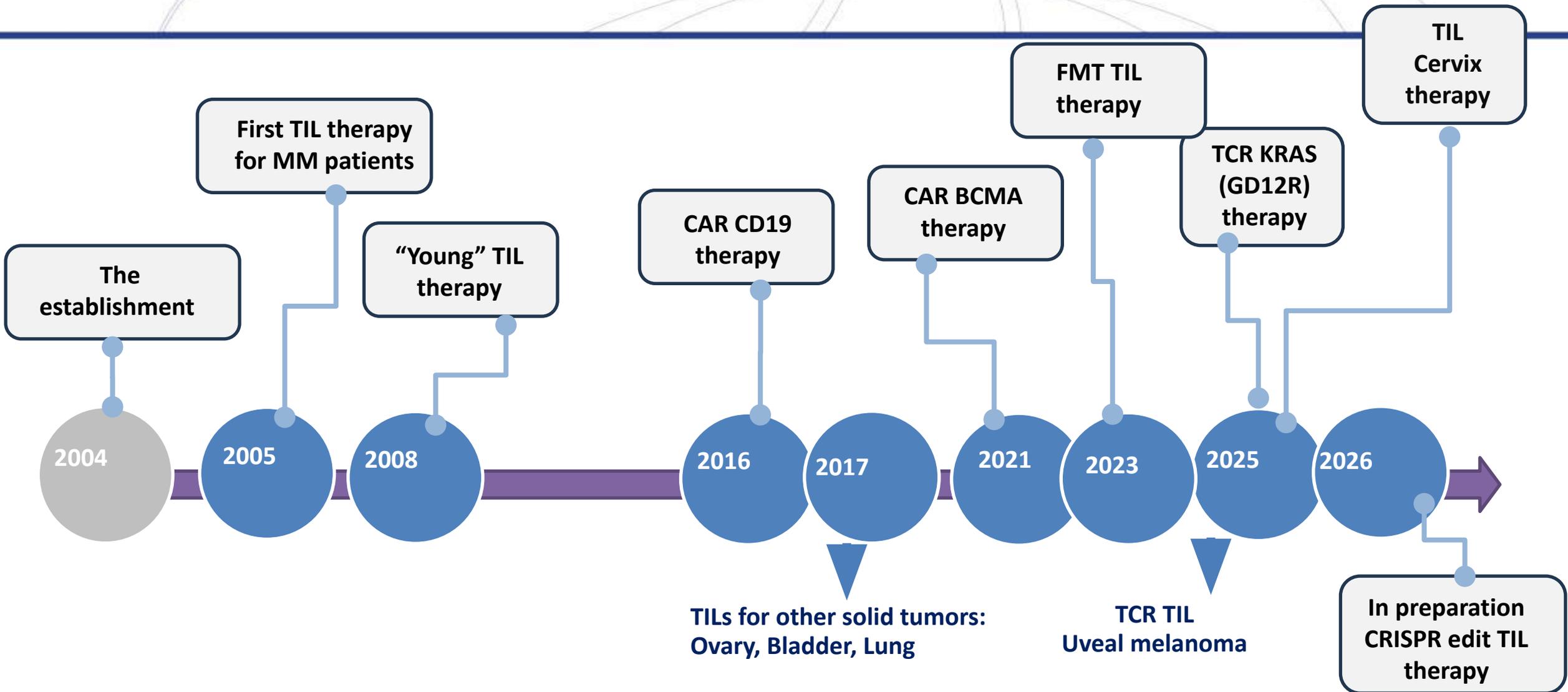


Sheba Medical Center  
Climbs to #8



World's Best Hospital 7 Consecutive Years!

# The development of the Ella Institute over the years



## Clinical Trials at Sheba for CAR T-Cells

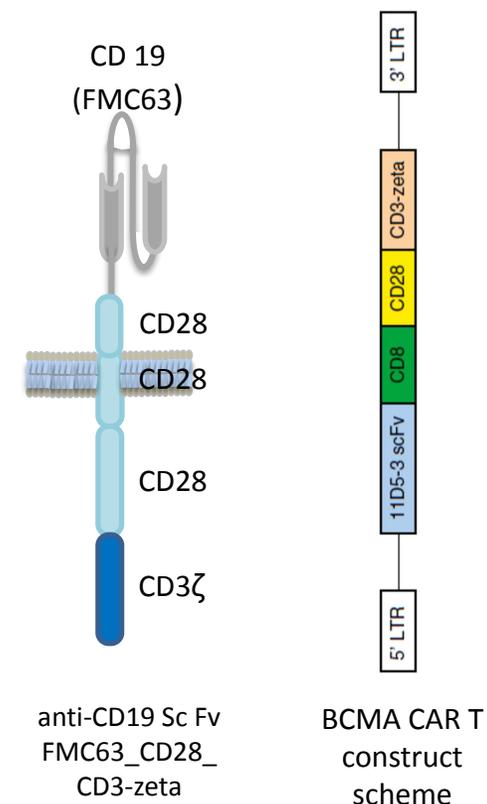
- **NTC02772198: A Phase 1b/2 trial ,CAR T CD19 for relapsed/refractory (R/R) blood cancers (since 2016).**
- **NCT04257175: CAR-T CD19 for Acute Myeloid Leukemia (AML), (since2020).**
- **NCT05243212: A Phase 1/2 trial of CAR-BCMA, for Multiple Myeloma (since 2021).**

### Autoimmune Diseases (Pioneering Research)

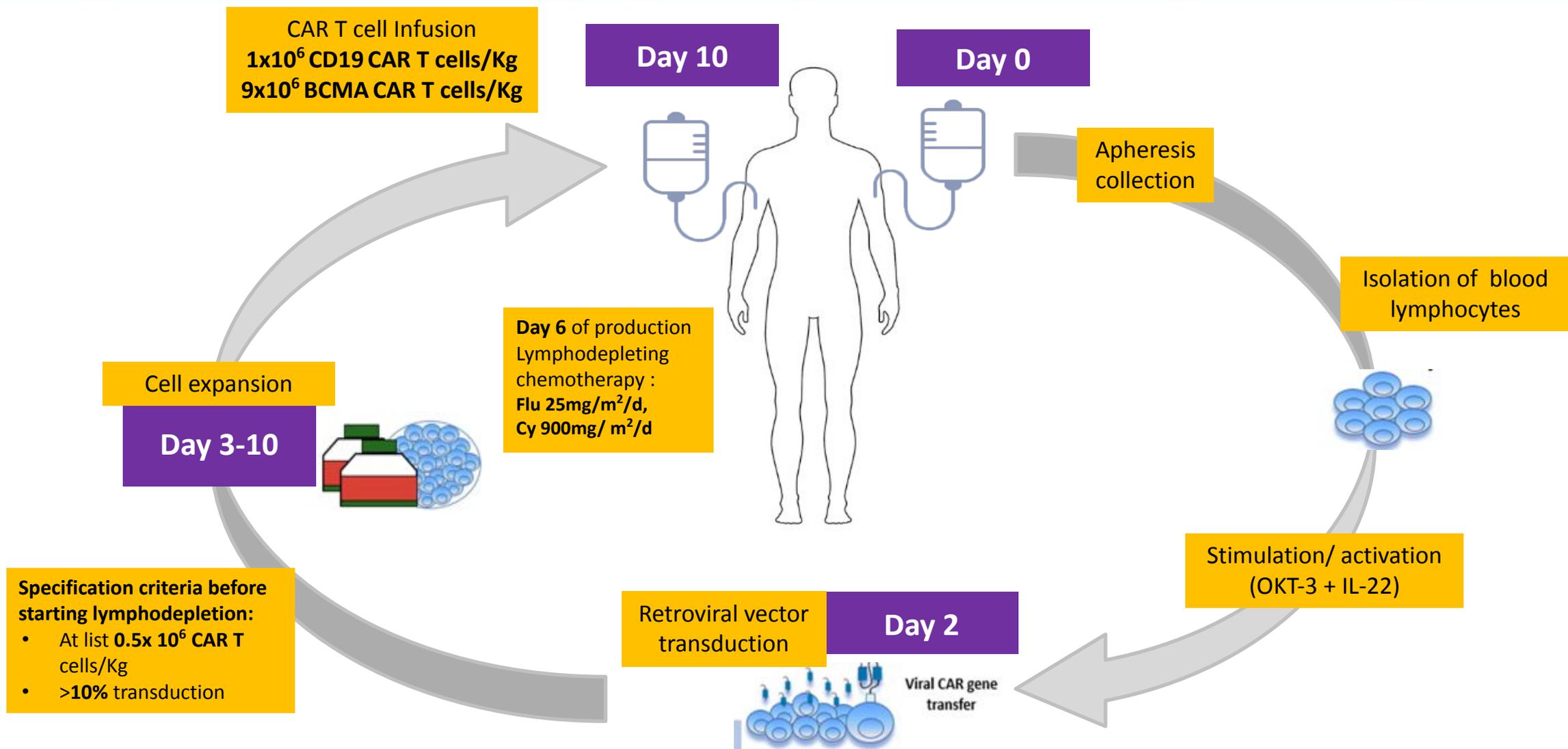
CAR T-cell program has expanded significantly in 2025 to treat severe, treatment-resistant autoimmune disorders.

Typically for patients that have failed 2–3 prior lines of conventional therapy.

- Systemic Lupus Erythematosus (SLE)
- Rheumatoid Arthritis
- Systemic Sclerosis (Scleroderma)
- Dermatomyositis and Vasculitis



# Manufacturing Process for CAR T Cells



# Point-of Care Manufacturing of Autologous CD19 CAR T-Cells for R/R CD19+ Malignancies, from 2016 to 2025

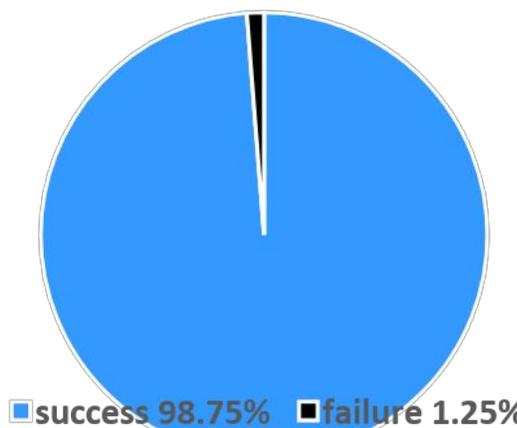
**Adult cohort:**  
**322 patients**  
**Pediatric Cohort:**  
**78 patients**

**Total treated patient: 371**  
**Total discontinuation: 27**  
  
Clinical deterioration: 22  
Production failure: 5

**400**  
Patients  
enrolled

- Overall cohort across all CD19-positive diseases - approx. **70%** response
- Long-term outcomes are comparable to those reported with commercial products.
- Well tolerated in patients (DLBCL, FL and B-ALL)

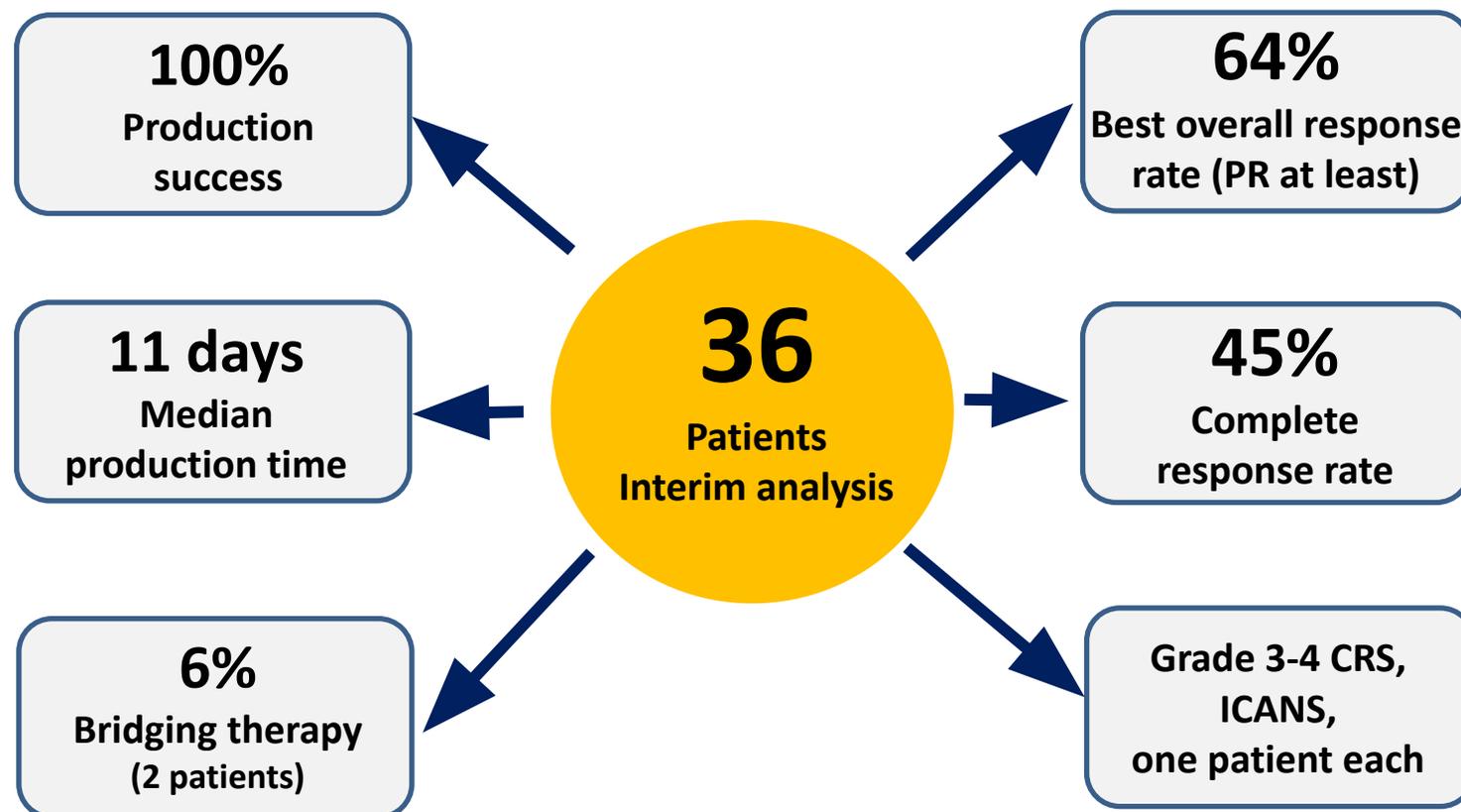
## Manufacturing success



S. Fried et al. Leukemia & Lymphoma, 2023, Vol. 64, No. 12, 1956–1963.  
M. Kedmi et al. Transplantation and Cellular Therapy 28 (2022) 251-257.  
E. Jacoby et al. , Br J Haematol. 2022;197:475–481.

# Point-of-Care BCMA CAR T-Cell Treatment for R/R Multiple Myeloma

- 60 patients were treated Between Nov 2021 and Nov 2025
- Most of the patients with resistant myeloma with high-risk disease features.



# Point-of-Care Cell Therapy Program: Strengths and Weaknesses

## Advantages

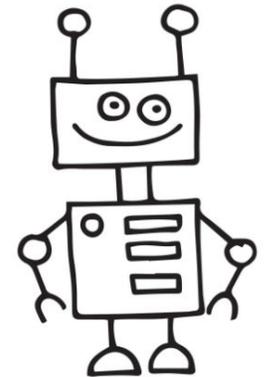
- Significant reduction of wait time
- Less bridging therapies
- Use of fresh cells
- Reduced logistics
- Expanded access –salvage therapy

## Drawbacks

- Manual open-system processing
- High personnel deployment
- High infrastructure demands
- Maintenance of consistent quality
- Regulatory hurdles

## Switching to closed-system automation to optimize quality, regulatory and cost concerns

- Cost efficiency
  - reduction of total labor cost
  - lower facility requirements
- Quality and scalability
  - reduction of human error
- Regulatory compliance
  - real time monitoring
  - digital audit trails
  - simplify regulatory documentation requirements
  - reduces the risk of non-compliance



## From Manual to Automated GMP Cell Manufacturing



### System highlights

#### •Single-Use, Closed System

- No cleaning, no cross-contamination, **reduced cleanroom demands.**
- Faster setup, safer operation.

#### •Scalable by Design

- From **20 million to 20 billion cells** with seamless scale-up.

#### •Regulatory Ready

- Full compliance with **cGMP** and **CFR 21 Part 11** data integrity.

#### •Remote Control

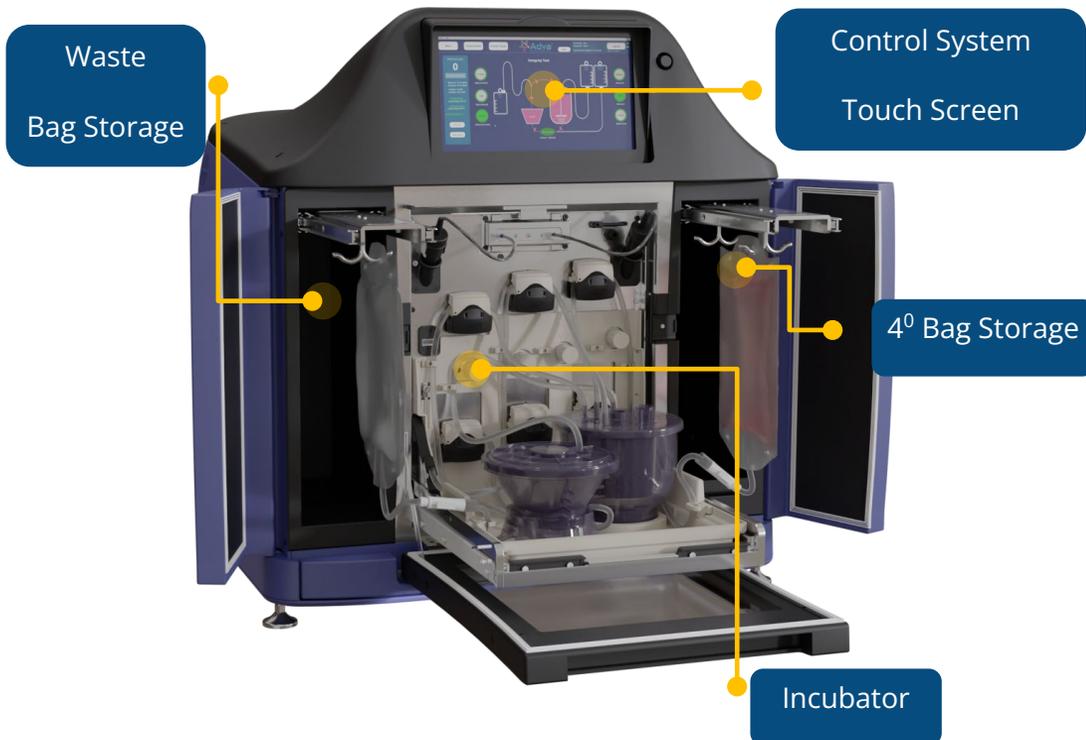
- 24/7 secure monitoring, alarms, and intervention from anywhere.



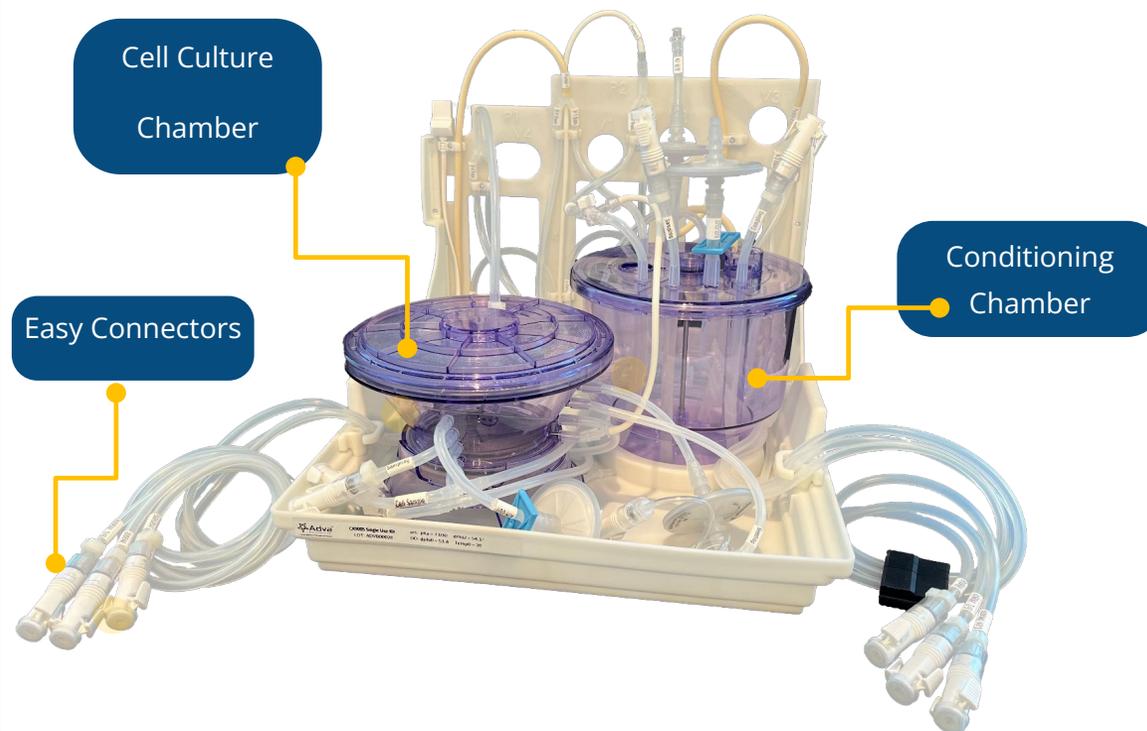
# ADVA SOLUTION

## Multiprocessor Unit With Single-Use Kits

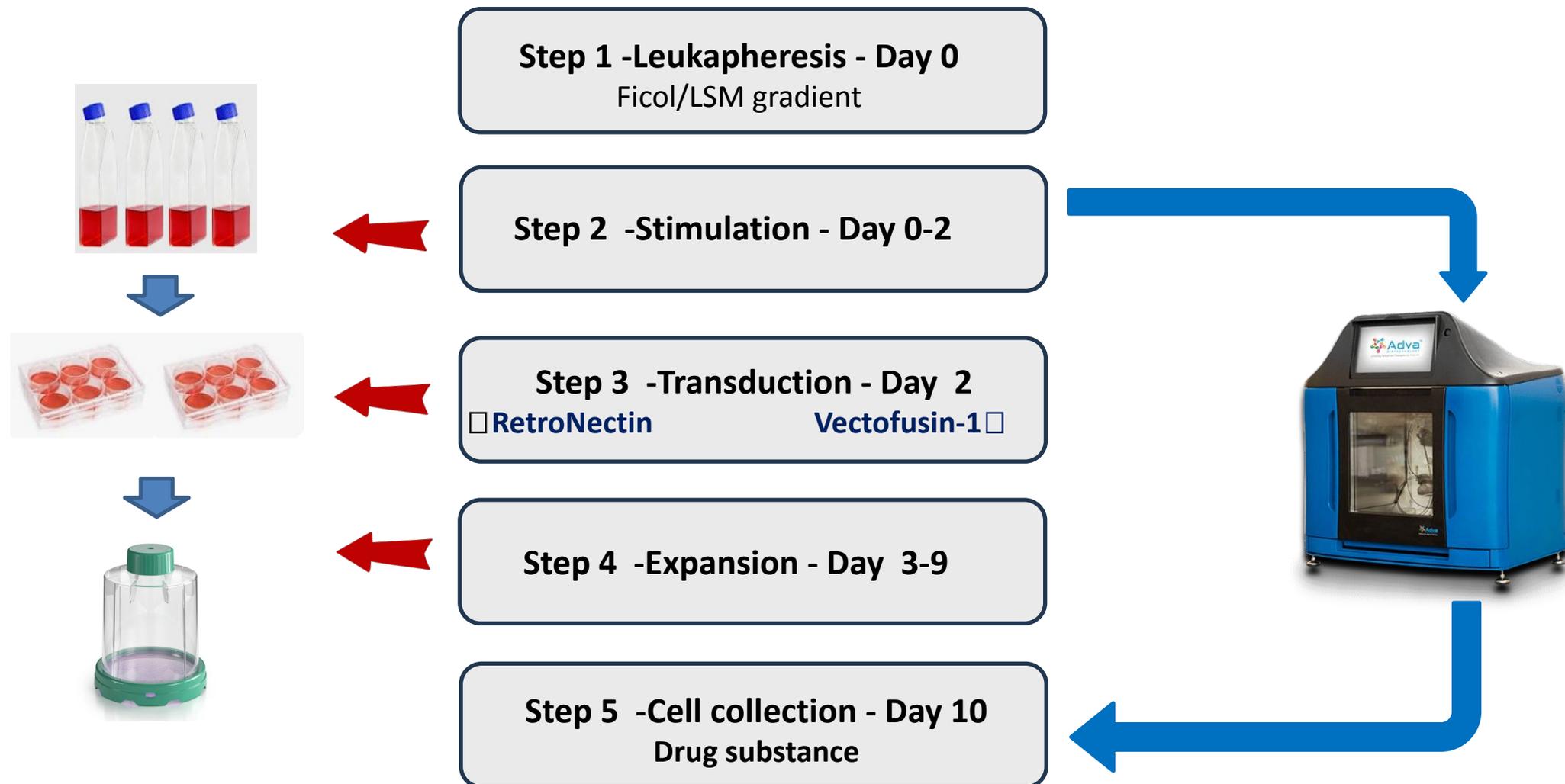
### ADVA *x3*<sup>®</sup>



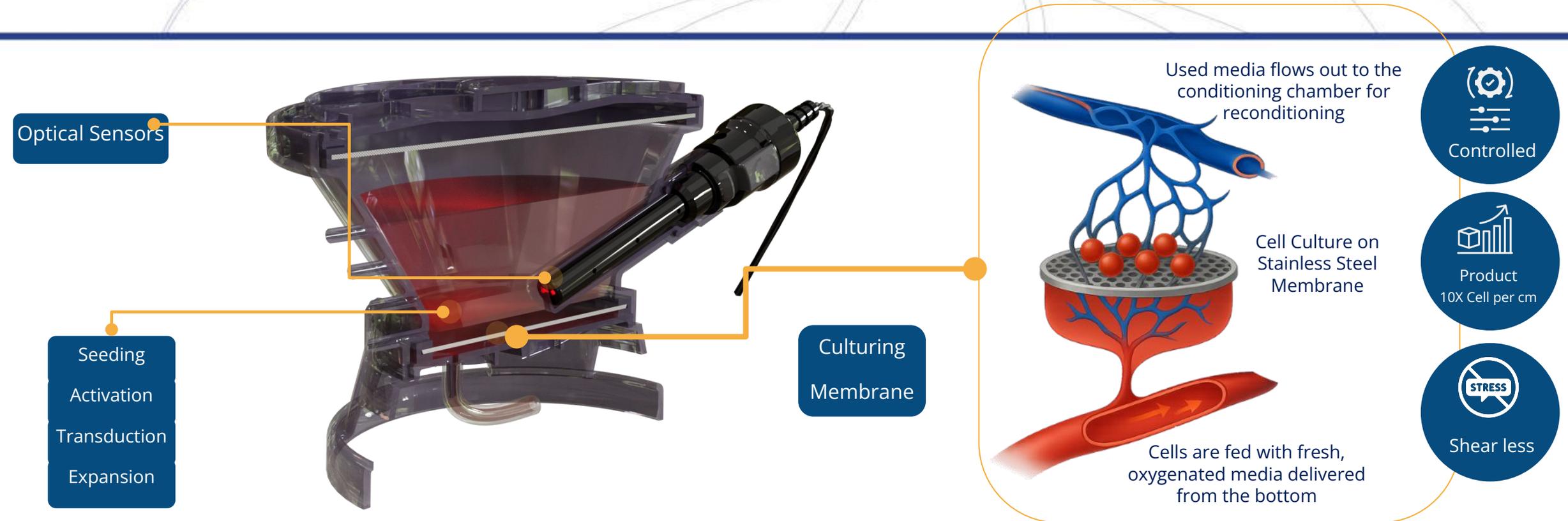
### CX900S – DISPOSABLE KIT



# Migrating the Manual CD19 CAR T-Cell Manufacture to **ADVA X3** Automated Platform



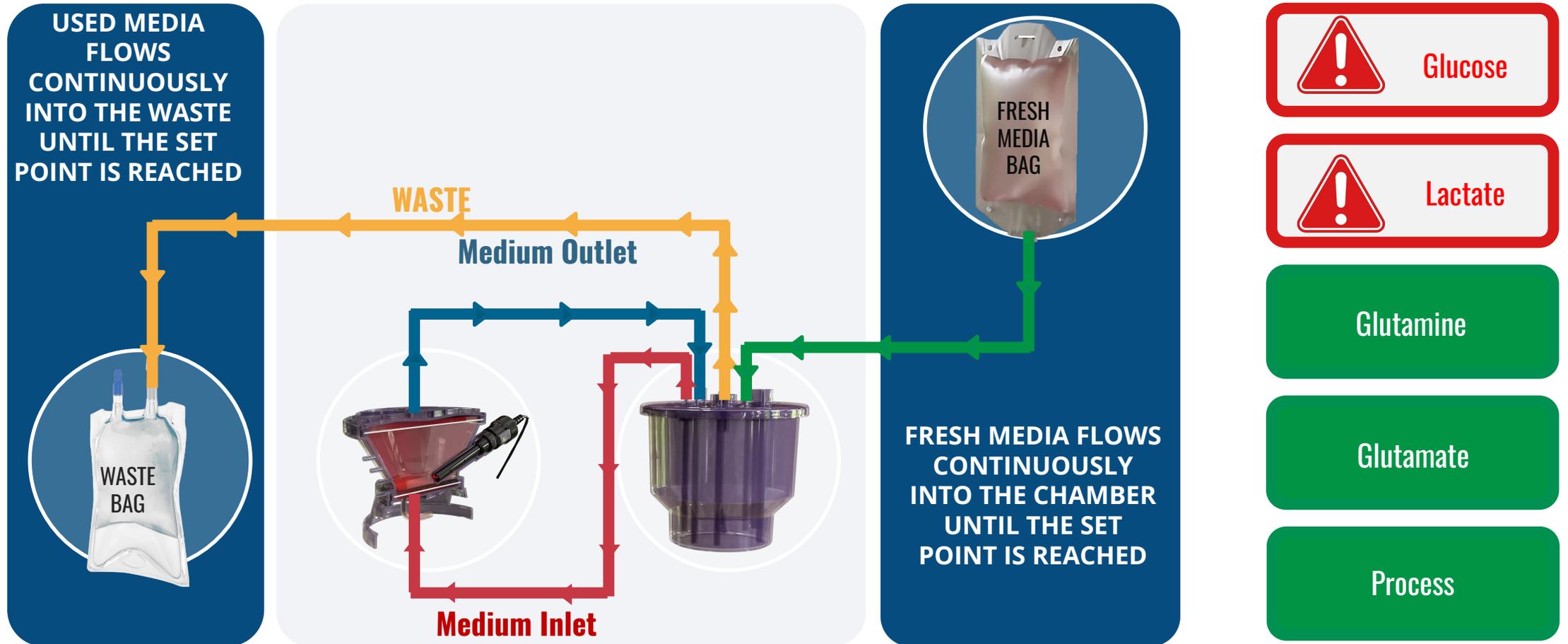
# ADVA CONE – Mode of Action and Flow Path



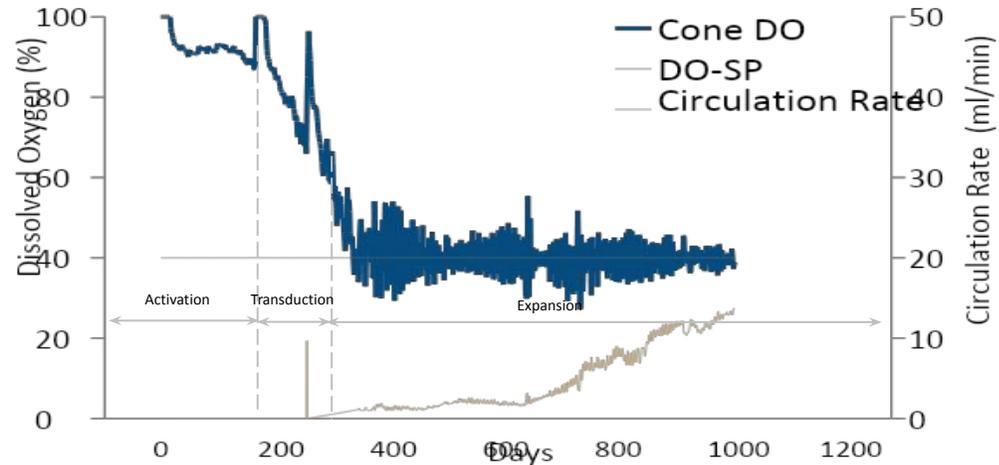
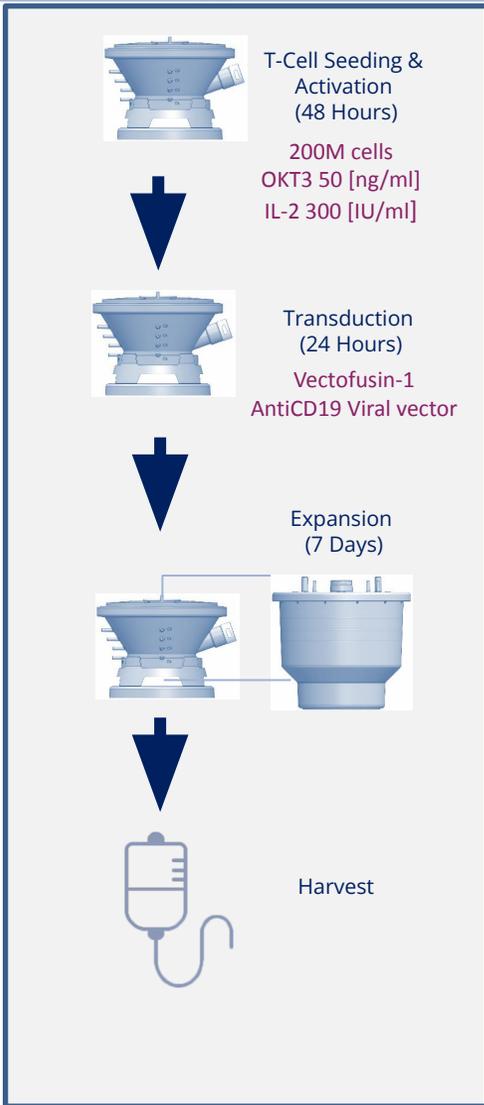
- Adva Biotechnology proprietary structured membrane allows media to flow from bottom to top, creating a uniform, shear-free diffusion environment.
- This design feeds cells with optimal nutrients, mimicking the natural flow dynamics found in the human body

# Control Scheme

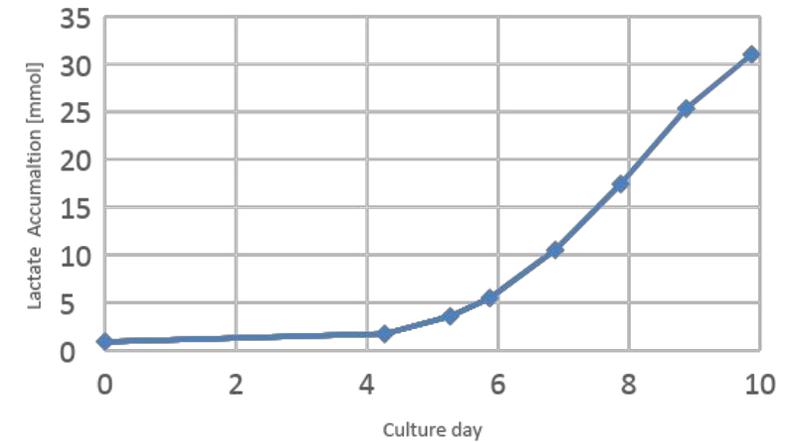
## Full/Periodical Perfusion Mode



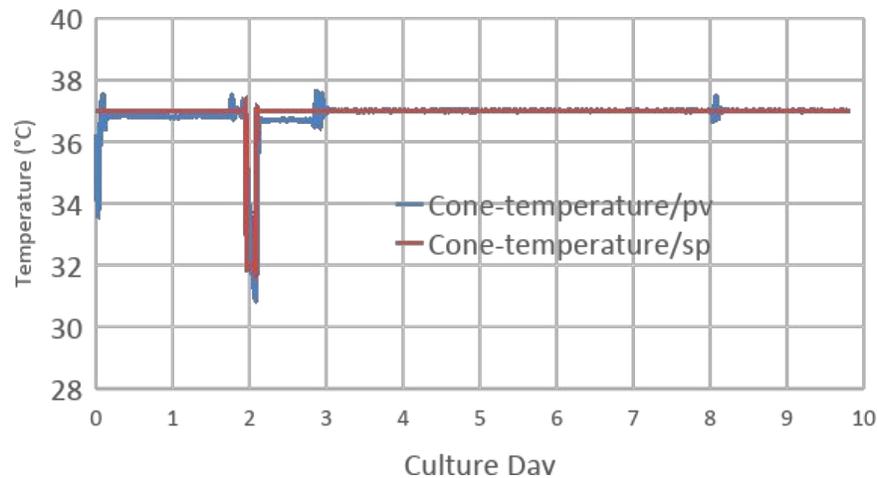
# Real-Time Monitoring of Automated CD19 CAR T-Cell Manufacturing



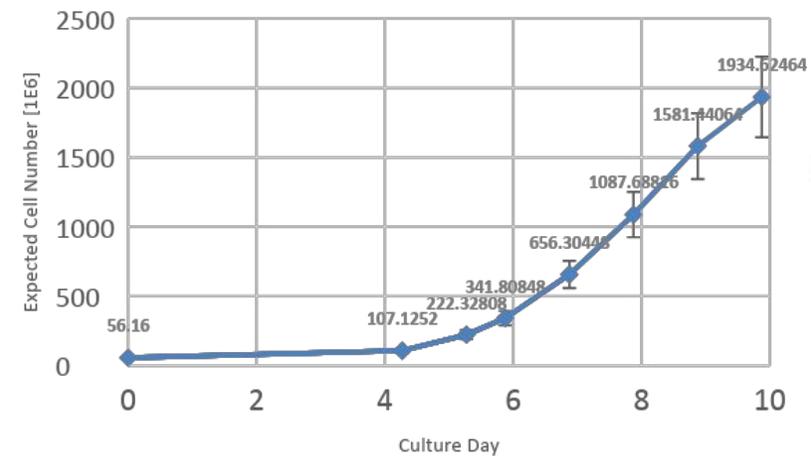
Run#9



Cone Temperature RUN#9

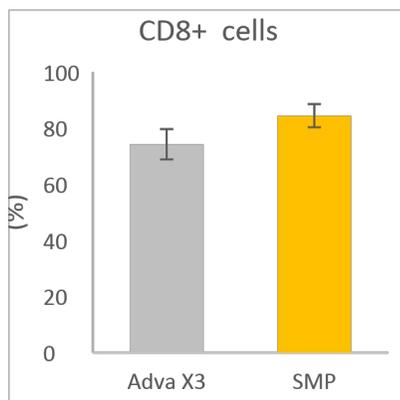
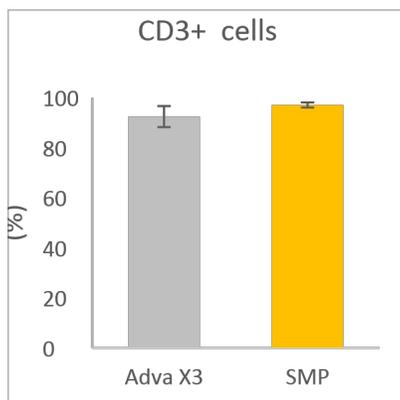
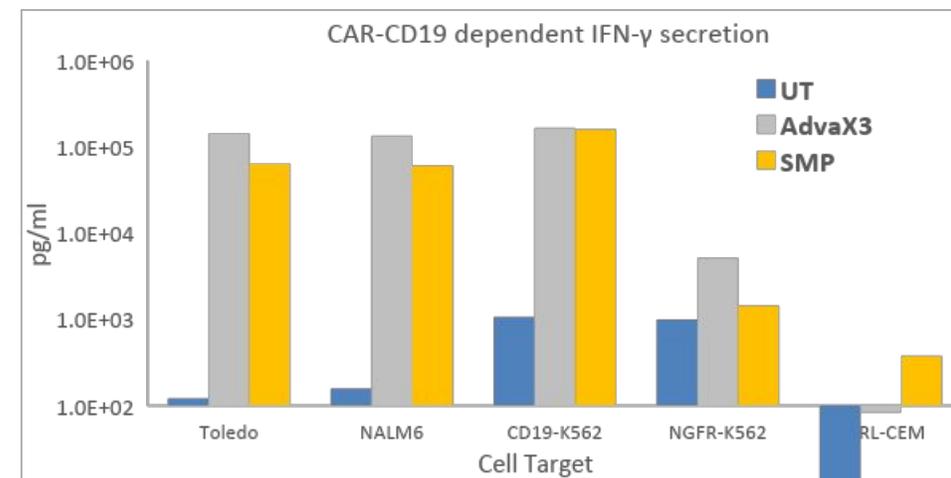
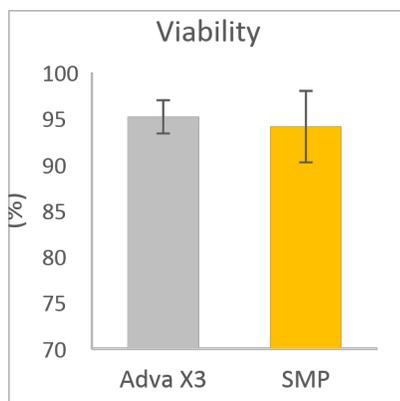
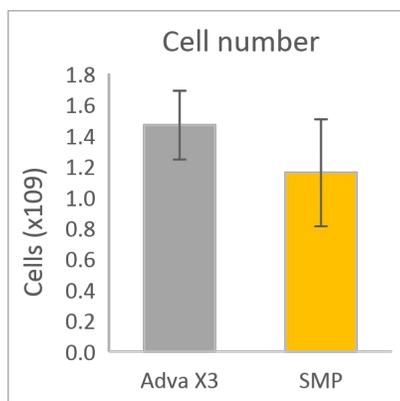


RUN#9



# CD19 CAR T Cells Manufacture

## ADVA X3<sup>®</sup> vs Manual Performance



SMP	AdvaX3	
66.05 ± 2.58	28.48 ± 6.18	TD efficacy *
2.69 ± 0.84	1.30 ± 0.24	VCN

# Summary of Autologous CAR T-Cell Manufacturing in

**ADVA X3<sup>®</sup>**

ADVA X3 Run#1	ADVA X3 Run#8	ADVA X3 Run#7	ADVA X3 Run#6	
417-MM	415-PD	404-KH	199-AR	Donor -Patient
FL	B-ALL	Burkit L	FL	Disease
fresh	fresh	frozen	frozen	Cells
200E6	200E6	200E6	200E6	Seeding Cells no.
7	7	8	8	Expansion Days
2,500 E6	1,049 E6	2,730 E6	1,968 E6	Harvest cell no.
95.5%	96.0%	96.7%	92.6%	Cell Viability
96.6%	93.8%	80.3%	99.2%	CD3+
37%	40.4%	14.1%	22%	Transduction efficacy
930 E6	420 E6	380 E6	430 E6	Total CAR T cells
50 E6	116 E6	60 E6	64 E6	CAR T cells required for therapy
		✓	✓	✓ In-spec ✓

# ADVA X3 - Industrial



 **Thanks**

## Ella Lemelbaum Institute

### Laboratory Team



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