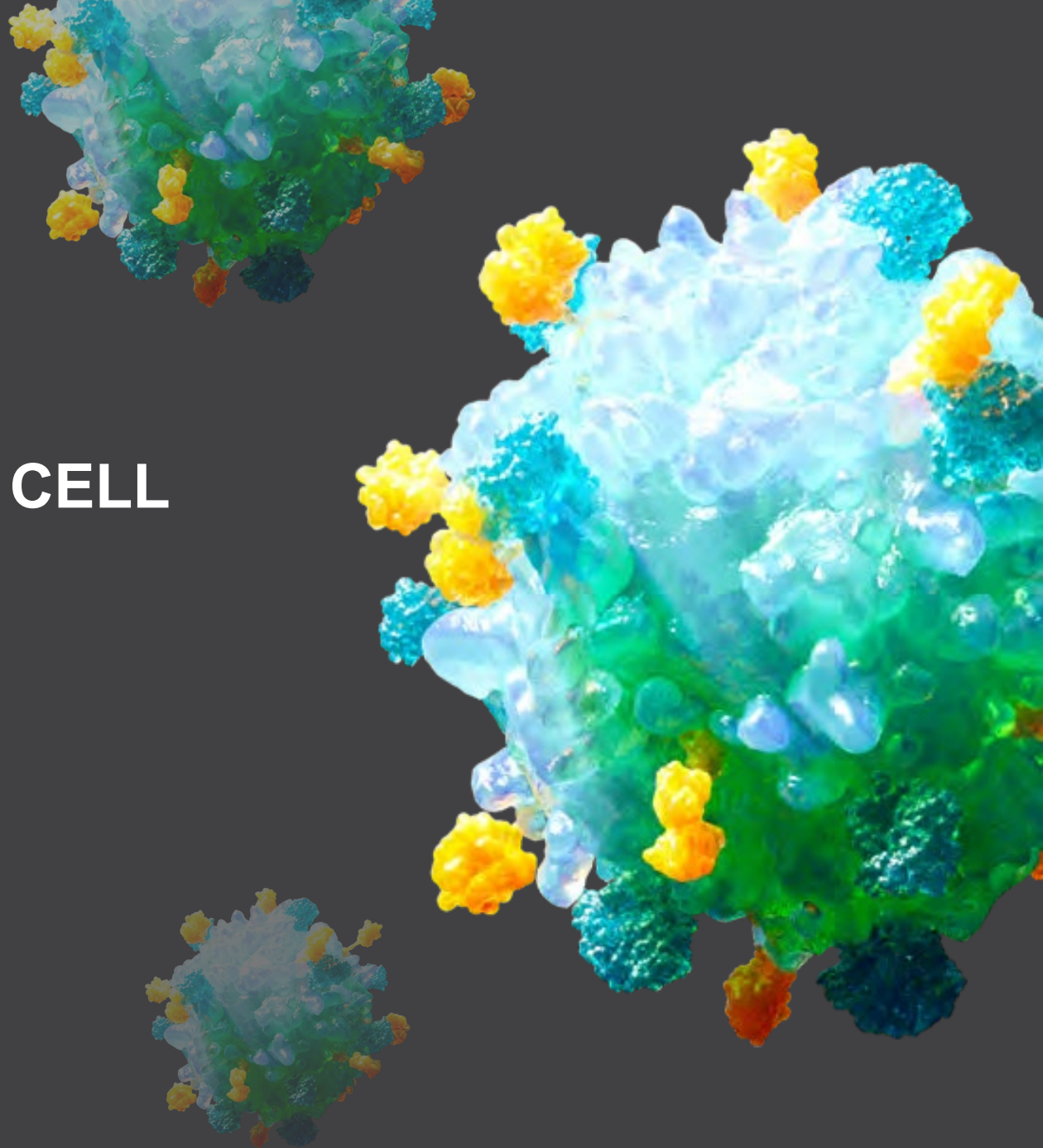




# UNLEASHING THE PROMISE OF CELL THERAPY FOR CANCER AND AUTOIMMUNE DISEASES

SEP 9, 2024

Nasdaq: ATRA



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# Atara Biotherapeutics is Focused on Natural T-Cell Biology with a Differentiated, Off-the-Shelf Approach

## Atara Overview

- Company founded in 2012
- Headquartered in Thousand Oaks, CA with ~165 employees
- First company to obtain regulatory approval for an allogeneic T-cell immunotherapy with EBVALLO™
- Novel platform leverages the unique biology of Epstein-Barr virus (EBV) T cells, a type of alpha beta T cell
- Capability to leverage this platform to treat a range of serious diseases through selective addition of chimeric antigen receptors (CARs)

## Atara's Allogeneic CAR T Programs

### B-cell Driven Autoimmune Diseases

#### ATA3219

CD19 CAR:

*Lupus Nephritis and Severe Systemic Lupus Erythematosus Study Initiation Expected Q4 2024; Initial Clinical Data Expected Mid-2025*

### Hematological Malignancies

#### ATA3219

CD19 CAR:

*Initial NHL Ph1 Data Expected Q1 2025*

#### ATA3431

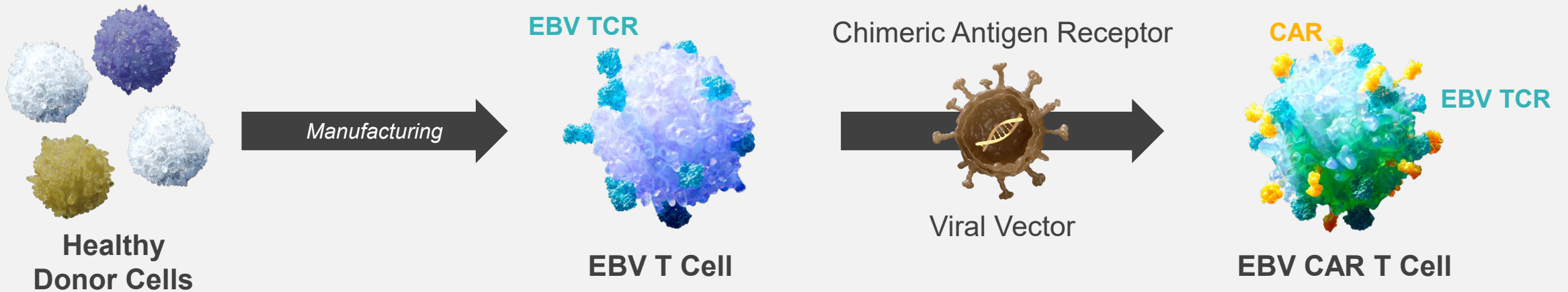
CD19/20 CAR:

*IND Targeted for H2 2025*

# Innovating Next-Gen CAR T Leveraging the Only Allogeneic T-cell Platform With an Approved Product

## Allogeneic EBV T-Cell (EBVALLO™)

## Next-gen Allogeneic CAR T



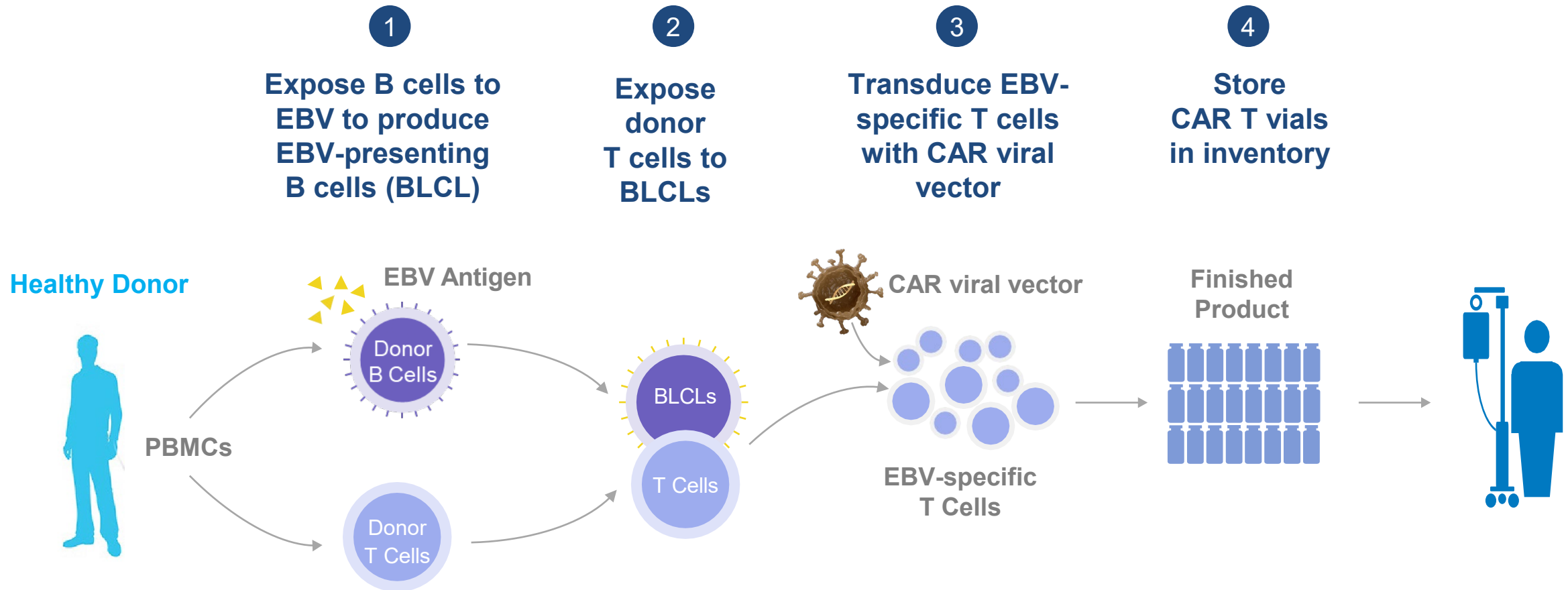
- ✓ No gene editing of the TCR or MHC
- ✓ Minimal HLA matching (only 2 of 10 alleles)
- ✓ No lymphodepletion
- ✓ Favorable safety profile in 600+ patients with outpatient experience
- ✓ Robust manufacturing with biologic-like COGM

- ✓ Retain features of EBV T cells
- ✓ Does not require complex gene edits
- ✓ Leverages novel CD3ζ signaling domain
- ✓ CAR-targeted activity – can be modified to express single or dual targets

EBV = Epstein-Barr Virus; HLA = Human Leukocyte Antigen; CAR = Chimeric Antigen Receptor; TCR = T-cell Receptor; MHC = major histocompatibility complex

Tab-cel® (Ebvallo™) is approved in the European Union

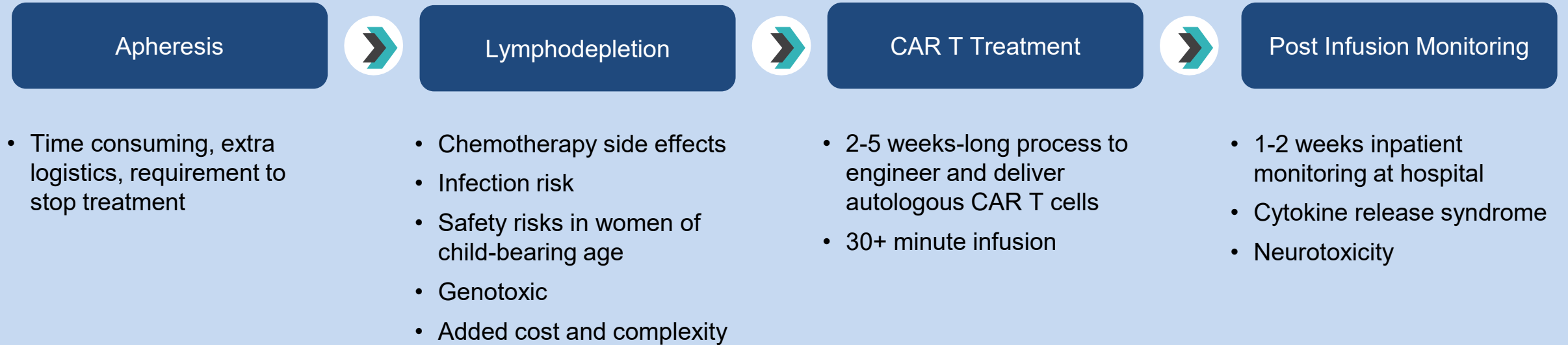
# Atara's Allogeneic CAR-T Manufacturing Process Leverages Our Commercial Manufacturing Process for Tab-cel



EBV = Epstein-Barr Virus; PBMC = peripheral blood mononuclear cell; BLCL = B lymphoblastoid cell line

# Atara's Allogeneic CAR T Platform Designed to Improve Patient Journey and Expand Access Versus Autologous Cell Therapies

## Current Autologous CAR T Patient Journey

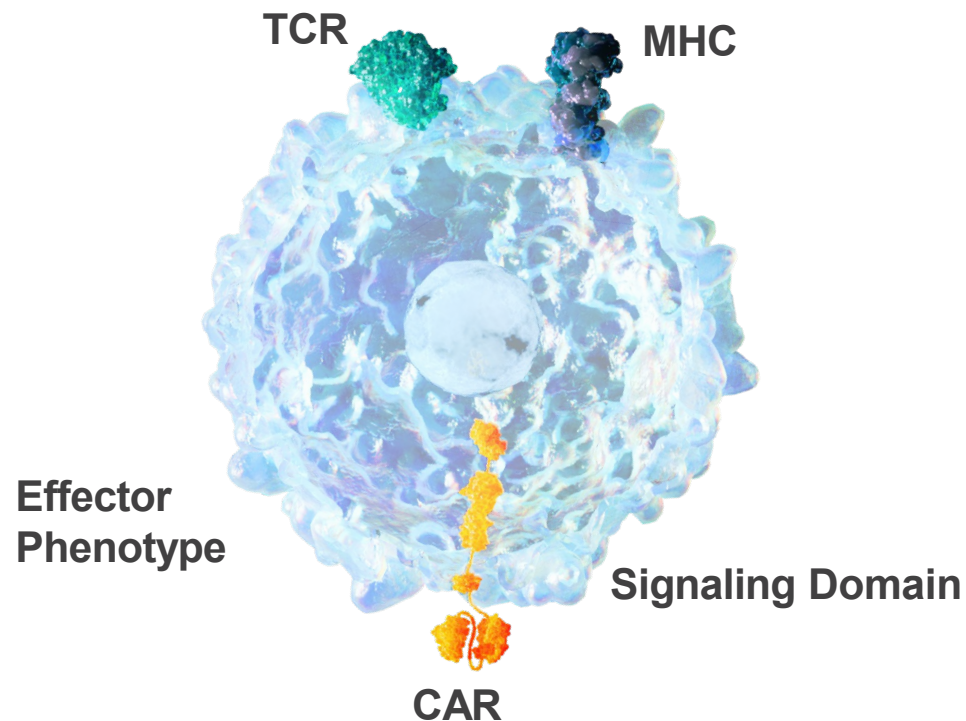


## Atara T Cells Offer Unique Potential Advantages in the Allogeneic Field (as evaluated in tab-cel & ATA188 clinical development studies)



# Allogeneic Requires a Different Approach to Overcome Key Challenges

## Conventional $\alpha\beta$ CAR T



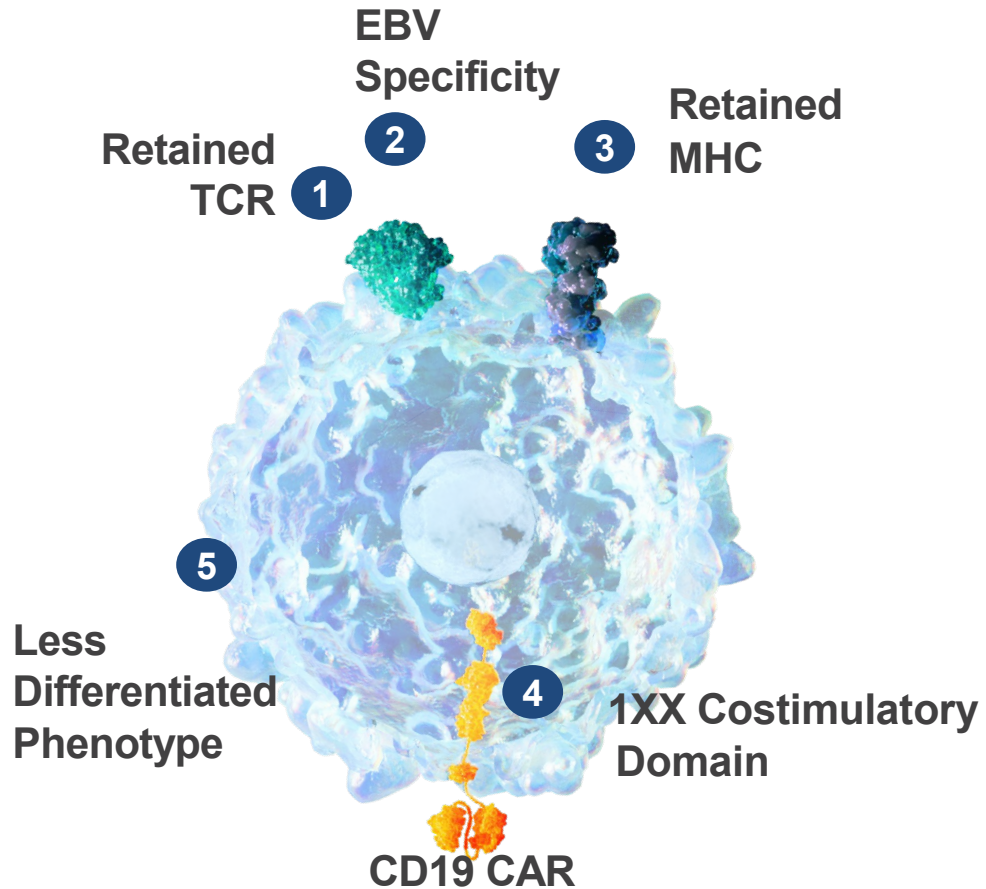
TCR = T-cell receptor; MHC = major histocompatibility complex;  $\alpha\beta$  = alpha beta; Graft-versus-host disease (GVHD)

## Key Challenges to Overcome

- **Graft vs Host Disease and Allojection:** Requires genetic alterations to TCR and MHC. Deletion of MHC also increases NK-cell-mediated CAR-T destruction
- **Exhaustion and Diminished Persistence:** Redundant CAR CD28 and CD3 $\zeta$  signaling can lead to over-activation and T-cell differentiation away from memory programs
- **Inflammatory Response:** Differentiated CAR-T cells exhibit more immediate expansion *in vivo*, faster time to peak T-cell concentration, and more severe cytokine-based inflammatory reactions

# Atara's CAR T Platform Combines the Natural Biology of T Cells With the Benefits of an Allogeneic Therapy

## Atara's Allogeneic CAR T Platform



TCR = T-cell receptor; MHC = major histocompatibility complex;  $\alpha\beta$  = alpha beta; Graft-versus-host disease (GVHD)

## ATA3219 Key Features

### Graft vs Host Disease (GvHD) and Allorejection:

- 1 **Retained TCR:** Unedited TCR serves as a key T cell survival signal<sup>1,2,3</sup> contributing to functional persistence<sup>3</sup>
- 2 **EBV Specificity:** Low GvHD risk due to TCR recognition of viral antigens
- 3 **Retained MHC:** Partial HLA matching<sup>4</sup> enables allogeneic approach that avoids host versus graft rejection<sup>5</sup>

### Exhaustion, Diminished Persistence, and Inflammatory Response:

- 4 **1XX Costimulatory Domain:** Novel CD3 $\zeta$  signaling domain<sup>6</sup> optimizes potency, expansion and mitigates T-cell exhaustion while modulating activation
- 5 **Less Differentiated Phenotype:**  $\alpha\beta$  T-cell manufactured with less differentiated phenotype contributes to potency and moderates *in vivo* expansion of CAR-T cells, translating to potentially less severe inflammatory reactions



# Clinical CAR T Data From Industry Leaders and Academia Reinforce Key Features of Atara's CAR T Platform in Oncology and Autoimmune Diseases

**EBV Specific TCR & Retained MHC with Partial HLA Matching**

*Safety and persistence*

**Memorial Sloan Kettering**  
Allogeneic EBV CD19 CAR T

Overall survival up to 3 years in post-transplant B-cell malignancy patients with favorable safety profile (0.7 x 10<sup>6</sup>/kg per dose, n=12)<sup>1</sup>

**Less Differentiated Phenotype**

*Durability and potency*

**YTB-323**

Stem-enriched auto CD19 CAR T

73% CRs, 62% durable CRs at 6 months (12.5M DL2, n=30)<sup>3</sup>

Preliminary safety and efficacy in 3 SLE patients<sup>4</sup>

**1XX Costimulatory Domain**

*Expansion, persistence and potency*

**TAK-940**

CD19 auto CAR T with 1XX

ORR 87%, CR 75% (25M DL1, n=16)<sup>2</sup>

# ATA3219 in NHL: Opportunity To Compete With a Differentiated Profile Given Limitations With Other CD19-Targeted Therapies

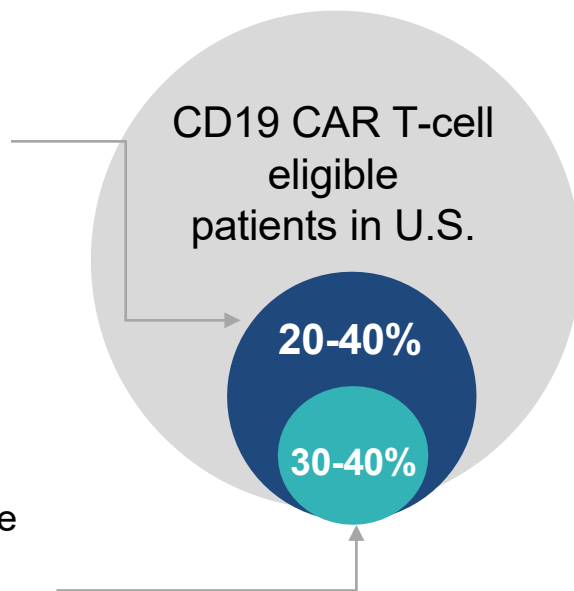
## Unmet Need Despite Approved Auto CAR T

### Access challenges for auto CAR T

Only ~20-40% of eligible patients receive CAR T therapy<sup>1,2</sup>

### Durability challenges for auto CAR T

Only ~30-40% of those who receive autologous CD19 CAR T therapy have durable response at 6 months<sup>3†</sup>



## Bispecifics & Allo CAR Yet to Deliver

### Efficacy and safety challenges for bispecifics

Risk/benefit profile still challenging (CRS/ICANS), limited tissue penetration, incomplete B-cell depletion, limited durability of remission, and repeated administrations

### Durability and persistence challenges for allogeneic CD19 CAR cell therapy

Limited durability of remission with no clinically superior platform

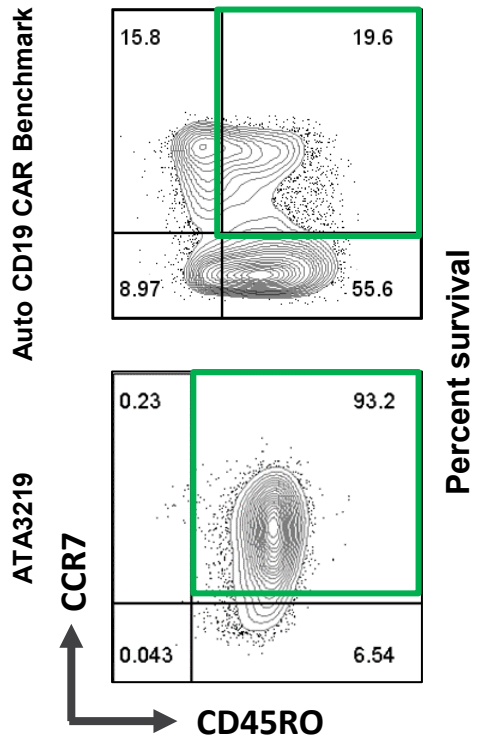
1. Geethakumari PR, et al. *Curr Hematol Malig Rep.* 2021;16(4):345-356. 2. Schuster SJ. *The Lancet. Oncology.* 2019; 20(1):2-3. 3. Atallah-Yunes SA, et al. *Frontiers in Immunology.* 2022; Volume 13. Note: Estimates for 2022 do not include full impact of ongoing 2nd Line CART utilization. †Estimate derived from PIs of approved auto-CAR T; includes reported and extrapolated information.

# ATA3219 in NHL: Potential "Best-in-Class" Profile with Superior *In Vivo* Persistence & Efficacy Versus Commercial Auto CD19 CAR T Benchmark

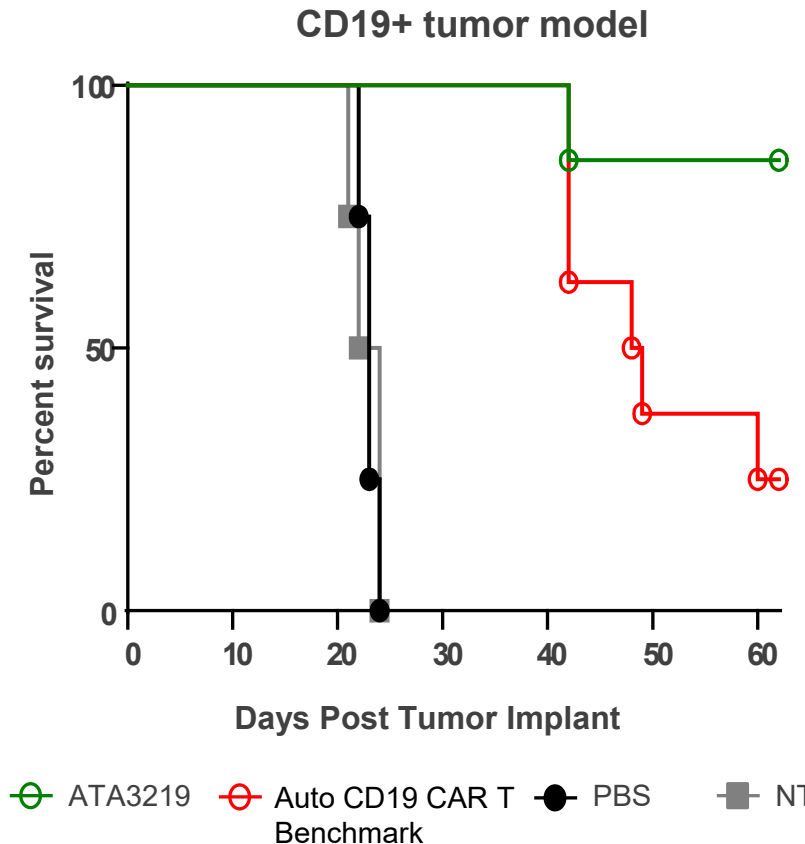
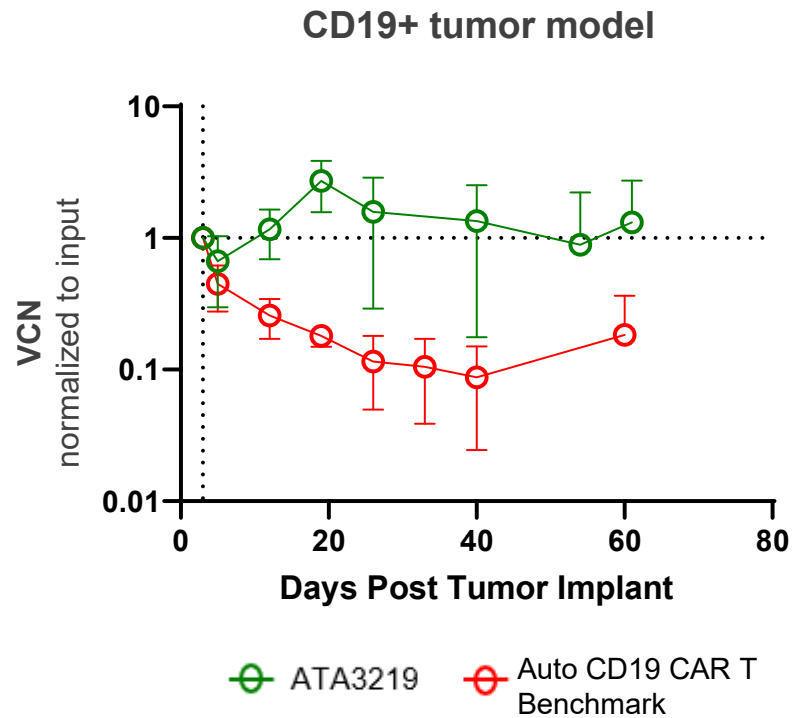
Less Differentiated T Cells for ATA3219

ATA3219 Longer Persistence versus auto CD19 CAR benchmark<sup>1</sup>

ATA3219 Superior Efficacy versus auto CD19 CAR benchmark<sup>1</sup>



Percent survival



1. Pham, C, et al. Abstract presented at Transplantation & Cellular Therapy (TCT) Meetings; 2023. Auto CD19 CAR T benchmark with CD28 and CD3ζ signaling domains. Note: T-cell infusion on day 3 day after tumor implantation (day 0); infusion timepoint represented as a vertical line on the center graph.

# SLE: High Unmet Need and Opportunity for CAR T Therapy



## High Unmet Need in Systemic Lupus Erythematosus (SLE)

- SLE is a chronic autoimmune inflammatory disease affecting multiple organs, with heterogeneity of clinical symptoms and disease severity making it difficult to treat<sup>1</sup>
- Unmet needs include uncontrollable disease, recurrent flares, need for long-term immunosuppressive treatment, increased rates of infections, damage accrual that impairs quality of life, and diminished long-term survival<sup>2</sup>



## Targeting B Cells with CAR T Therapy to Achieve Remission

- B cells play a pivotal role in the pathogenesis of SLE<sup>2</sup>
- In an academic study of autologous CAR T cell therapy in lupus, 8/8 patients with >1 year post CAR T therapy follow up achieved durable, drug free remission<sup>3</sup>
- Lymphodepletion free approaches needed to minimize toxicities, logistical complexities, hospitalization, costs, and enable increased CAR T access for autoimmune patients

**ATA3219: Designed to achieve deep B-cell depletion and immune system reset in lupus**

1. Katarzyna, PB. et al. Current treatment of systemic lupus erythematosus: a clinician's perspective. Rheumatol Int 43, 1395–1407 (2023).; 2. Yemil Atisha-Fregoso et al. Meant to B: B cells as a therapeutic target in systemic lupus erythematosus. J Clin Invest. 2021; 3. Mueller et al, ASH 2023.

# The Goal of CAR T Mediated B-Cell Depletion Is Drug-Free and Long-Term Responses for SLE Patients



**B- cell depletion**

**CAR T penetrates deep into tissues and rapidly depletes pathogenic CD19+ B cells**



**Immune system reconstitution**

**Immunological “reset” and reconstitution of naïve B cells lacking the autoreactive B-cell clones**



**Achieve remission**

**Reversal of disease and ability to achieve stable, long-term drug-free remission**

# ATA3219 Is Designed to Have a Best-in-Class CAR T Profile in Multiple Autoimmune Diseases

Atara's Differentiated T-Cell Platform



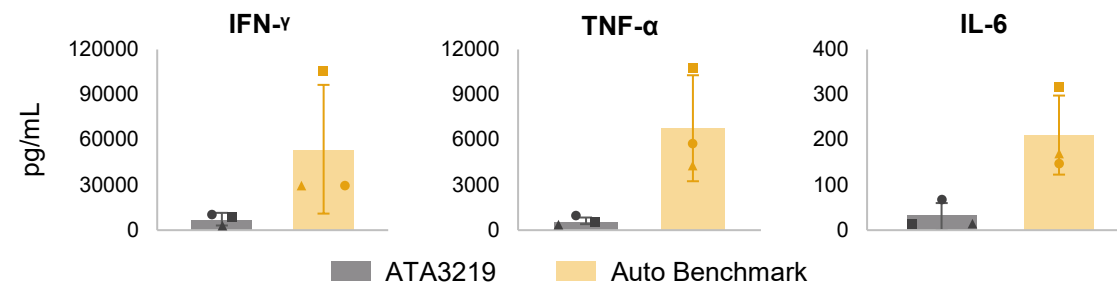
Allogeneic



Potential for Enhanced Efficacy, Tolerability and Patient Access

- Partial HLA matching
- EBV specific TCR with favorable safety in 600+ patients
- Memory phenotype
- 1XX costim domain
- $\alpha\beta$  T cells
- Tab-cel clinical data demonstrates efficacy in cell therapy treatment with no LD

- Off-the-shelf availability simplifies treatment
- Scaled-up manufacturing to address large populations
- No apheresis
- Lower COGS
- Healthy starting cells



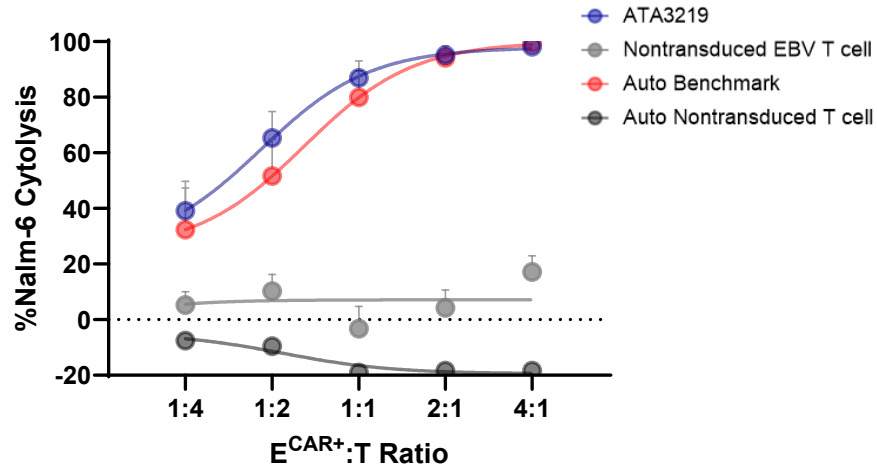
Preclinical data shows lower levels of pro-inflammatory cytokines vs autologous benchmark<sup>1</sup>

Atara pioneered allogeneic T-cell therapy with no lymphodepletion

# ATA3219 Maintains Comparable Cytotoxic Function With Reduced Inflammatory Cytokine Release Compared to Autologous Benchmark

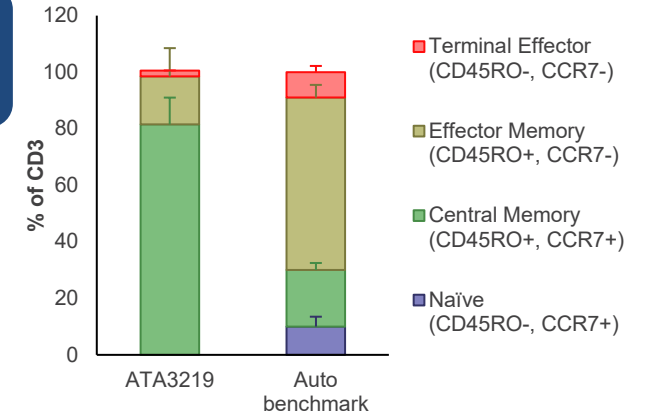
## % Cytolysis

*CD19-specific cytotoxic activity*



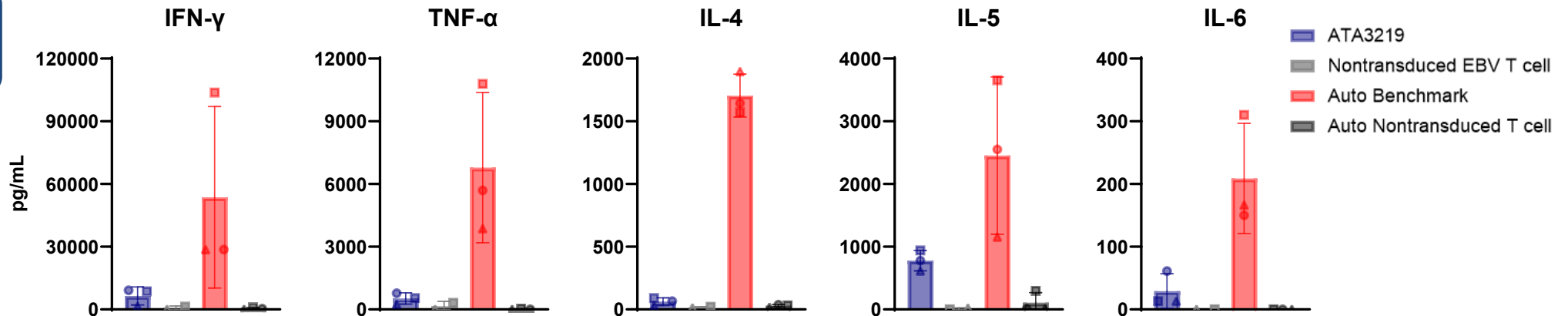
## Cell phenotype

*Maintained a robust central memory population*



## Cytokine Release

*Reduced inflammatory cytokine release*



ATA3219 and auto benchmark CAR T cells generated from the same three donors were co-cultured with Nalm-6 cells at a 3:1 E:T ratio for 24 hours. Supernatants were harvested and cytokine release was measured

# Rationale for No Lymphodepletion in Extrarenal SLE Cohort

## EBV T Cell

- **$\alpha\beta$  T-cell:** Same T-cell type as proven commercial autologous CAR Ts
- **Retained TCR:** T-cell survival signal contributing to persistence<sup>1-3</sup>
- **Specificity:** Low GvHD risk due to TCR recognition of EBV viral antigens
- **Tab-cel data:** Expansion and persistence without LD<sup>4</sup>

## Partial HLA Matching

- **Retained MHC:** Partial HLA matching limits host versus graft rejection<sup>5</sup>
- **Atara platform data:** Favorable safety profile seen in 600+ patients treated without lymphodepletion

## Additional Features

- **1XX costimulatory domain:** Optimizes potency and expansion and mitigates exhaustion<sup>6</sup>
- **Less differentiated phenotype:** Contributes to potency and durability of clinical response
- **ATA3219 data:** Less inflammatory cytokines in pre-clinical model versus benchmark autologous CD19 CAR T<sup>7</sup>

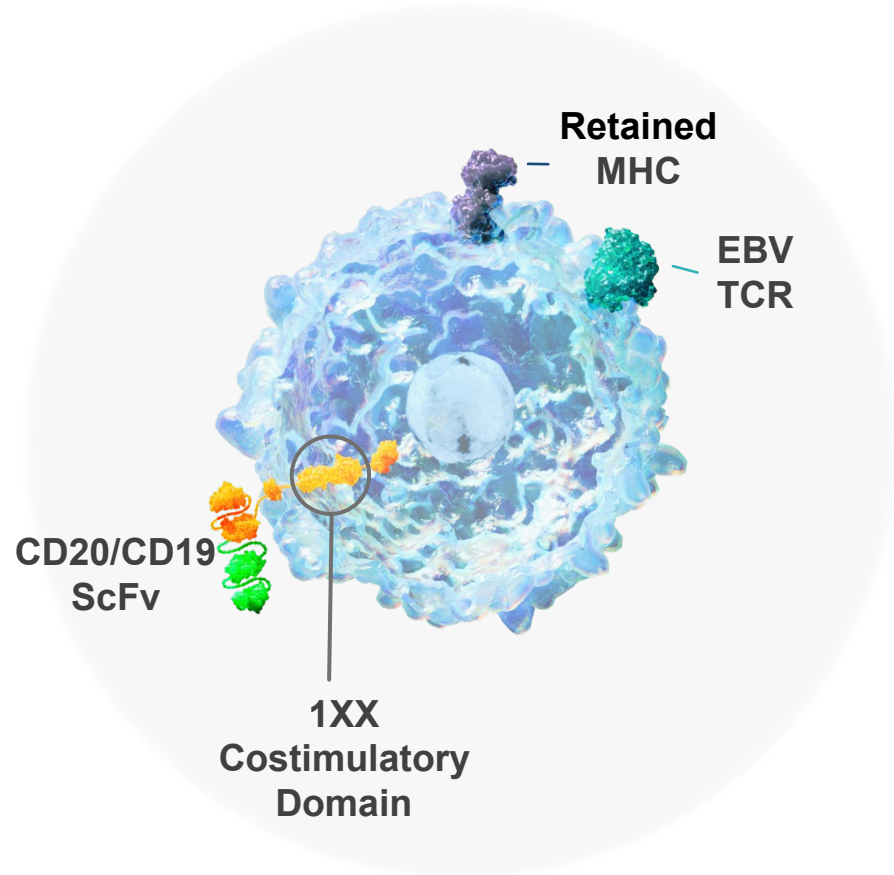
Achieving immune reset without lymphodepletion could improve tolerance and facilitate patient access

LD = lymphodepletion; HLA = human leukocyte antigen

1. Tanchot et al, Science 1997. 2. Myers et al, Trends Immunology 2017. 3. Polic et al, PNAS 2001. 4. Atara clinical experience; Prockop et al, JCI 2020. 5. Atara Data on file ATA129-EBV-302 Ph3 (DCO 9OCT2023). 6. Feucht et al, Nature Medicine, 2018. 7. Brito, A, et al. Poster presented at ISCT. 2024.



# ATA3431: Off-the-Shelf Allogeneic CD19/CD20 CAR T Program Progressing Toward IND Submission in H2 2025



Targeting CD19 and CD20 **reduces probability of relapse** due to CD19 antigen loss, hypothesized to be a major cause of treatment resistance or disease relapse after CD19 CAR T treatment



Targeting CD19 and CD20 provides **potential incremental efficacy benefit** and 1XX co-stimulation for **enhanced persistence**



Autologous CD19/CD20 dual CAR Ts have shown **promising efficacy** and **safety** in clinical trials (IMPT-314; C-CAR039<sup>1</sup>)



ATA3431 preclinical data demonstrates a competitive profile based on **potent** antitumor activity, **long-term** persistence, and **superior** tumor growth inhibition

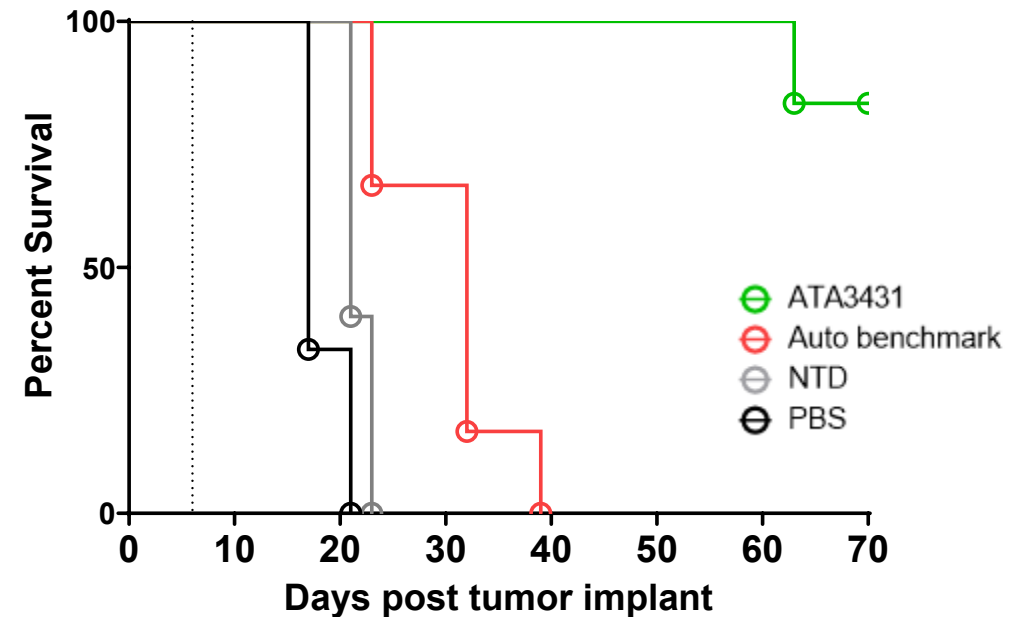
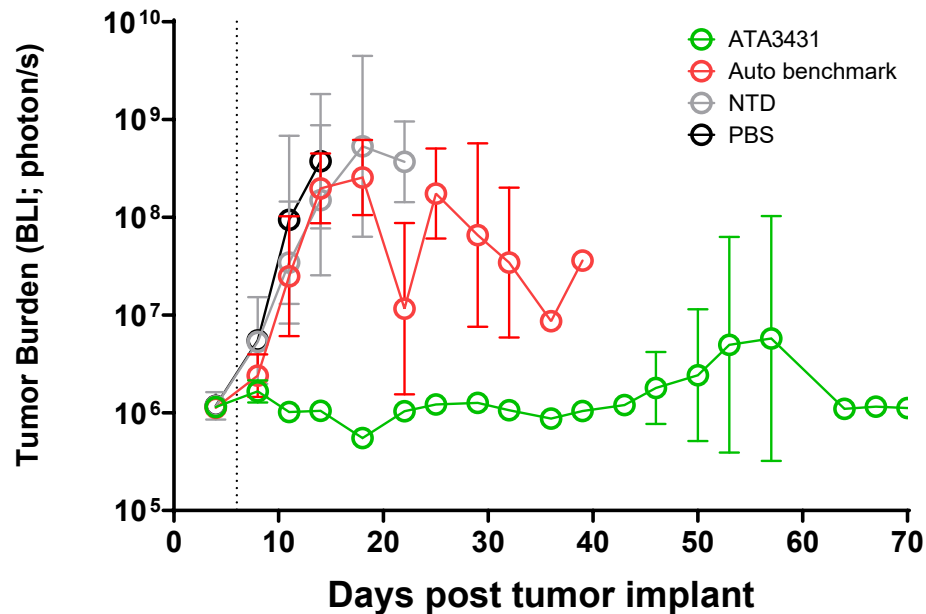
Positive preclinical data presented at American Society of Hematology meeting in December 2023<sup>2</sup>

1. Li, P, et al. C-CAR039, a Novel Anti-CD20/CD19 Bi-Specific CAR T-Cell Therapy Shows Deep and Durable Clinical Benefits in Patients with Relapsed or Refractory (r/r) B-Cell Non-Hodgkin Lymphoma (B-NHL) in Long Term Follow up. ASH 2023. 2. Cha, S et al. Poster 4800. ATA3431: Allogeneic CD19/CD20 Bispecific CAR EBV T Cells for the Treatment of B-Cell Malignancies. ASH 2023.

# ATA3431: Compelling Proof-of-Concept and Competitive Profile

## Greater Anti-Tumor Efficacy vs CD19/CD20 Autologous Benchmark

Challenging CD19<sup>low</sup> / CD20<sup>+</sup>  
Raji model



ATA3431 progressing toward IND submission in H2 2025

# Differentiated Allogeneic T-Cell Immunotherapy Pipeline

Program	Indication	Target	Preclinical	Phase 1	Phase 2	Phase 3	Registration	Next Milestone
ATA3219 (Oncology)	Non-Hodgkin's Lymphoma (NHL)	CD19	▶					<b>Q1 2025:</b> Initial NHL Ph 1 clinical data expected
ATA3219 (Autoimmune)	Lupus Nephritis (LN)	CD19	▶					<b>Mid-2025:</b> Initial LN Ph 1 clinical data expected
	Systemic Lupus Erythematosus (SLE) without lymphodepletion		▶					<b>Mid-2025:</b> Initial SLE Ph 1 clinical data expected
ATA3431	B-cell malignancies	CD19/CD20	▶					IND targeted for <b>H2 2025</b>
	Autoimmune disease		▶					
Tab-cel® or Eivallo™ (tabelecleucel)	RR EBV+ PTLD following HCT and SOT*	EBV	▶ ALLELE Study				EU Approved	BLA Accepted: PDUFA <b>Jan 15, 2025</b>
	Multi-Cohort (Label-Expansion): EBV+ cancers <sup>(1)</sup>	EBV	▶ EBVision Study					Ongoing enrollment
ATA188	Progressive MS	EBV <sup>(2)</sup>	▶ EMBOLD Study					Evaluating strategic options following completion of the study

Excluding Eivallo™ in EU, these investigational agents are not approved by any regulatory agencies and efficacy and safety have not been established

EBV+ PTLD: Epstein-Barr Virus Associated Post-Transplant Lymphoproliferative Disease; RR: rituximab relapsed/refractory; HCT: allogeneic hematopoietic cell transplant; SOT: solid organ transplant; NHL: non-Hodgkin's lymphoma

Atara has entered into an agreement with Pierre Fabre to commercialize tab-cel® for EBV+ cancers worldwide

\*Indication pursued as monotherapy for treatment of adult and pediatric patients two years of age and older with Epstein-Barr virus positive post-transplant lymphoproliferative disease (EBV+ PTLD) who have received at least one prior therapy. For solid organ transplant patients, prior therapy includes chemotherapy unless chemotherapy is inappropriate

Other programs: EBV vaccine and other hematological malignancies and solid tumor AlloCAR T programs

(1) Phase 2 multi-cohort initiated in Q3 2020, with possible indications including EBV+ PTLD with CNS involvement, front-line treatment in EBV+ PTLD including front line with CNS involvement, EBV+ PID/AID LPD, and other potential EBV-associated diseases

(2) Targeted antigen recognition technology; Phase 2 Randomized Controlled Trial

# Expanded Global Tab-cel<sup>®</sup> Partnership With Pierre Fabre Laboratories

Pierre Fabre Laboratories license for tab-cel global development, manufacturing and commercialization, with **up to \$640M** in potential consideration and **significant double-digit tiered royalties**

Substantially all tab-cel **clinical, regulatory and manufacturing activities** planned to transfer to **Pierre Fabre Laboratories** at time of BLA transfer



Atara received **~\$27M** following closing and **\$20M** following the positive pre-BLA meeting. Atara also received **\$20M** from the BLA acceptance with the potential to receive an additional **\$60** million milestone payment upon BLA approval

Pierre Fabre Laboratories to **reimburse Atara for tab-cel global development costs** through BLA approval, and **purchase manufactured tab-cel inventory** through BLA transfer

**Partnership will expand reach of tab-cel's life-saving potential to patients worldwide and provide future revenues for Atara**

# Tab-cel BLA Accepted With Priority Review and a PDUFA Target Action Date of January 15, 2025

The BLA is supported by pivotal and supportive data covering more than 430 patients treated with tab-cel across multiple life-threatening diseases

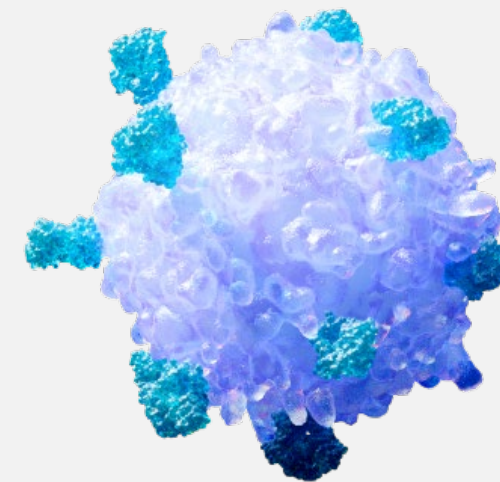
- The latest pivotal ALLELE study data demonstrated a statistically significant 48.8% Objective Response Rate ( $p < 0.0001$ ) and favorable safety profile consistent with previous analyses

## Unique approach to address rare and highly fatal cancer

- FDA Breakthrough Therapy Designation
- Orphan Drug Designation
- R/R EBV+ PTLD patients face a poor prognosis with median survival of only weeks to months
- No approved treatment options available

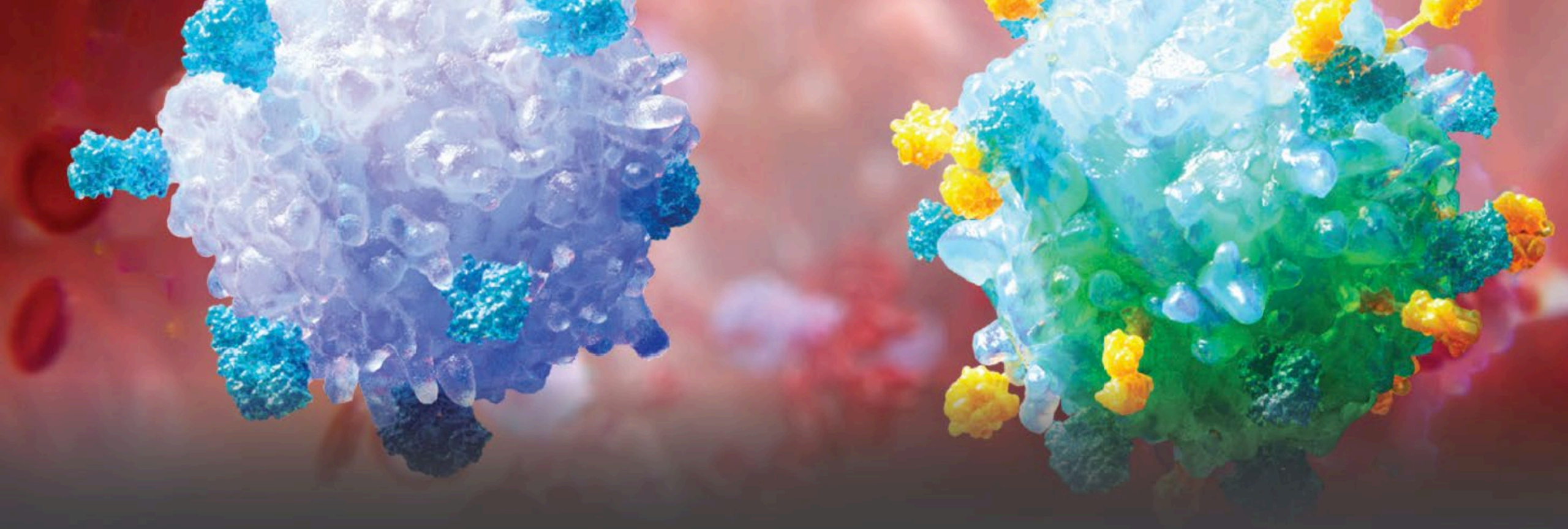
## Attractive Ultra-Rare Disease Market

- Few hundred patients per year in both U.S. and EU markets
- Potential label-expanding EBVision multi-cohort Phase 2 study enrolling
- Significant pricing potential with  $> \$500M$  in estimated peak sales



ORR – Objective Response Rate; DOR – Durability of Response; OS – Overall Survival

\*Indication pursued as monotherapy for treatment of adult and pediatric patients two years of age and older with Epstein-Barr virus positive post-transplant lymphoproliferative disease (EBV+ PTLD) who have received at least one prior therapy. For solid organ transplant patients, prior therapy includes chemotherapy unless chemotherapy is inappropriate



**THANK YOU**

*Nasdaq: ATRA*

