EXUMA Biotech

Architects of Cell Therapy

ADVANCED THERAPIES WEEK

January 19th, 2023

LIVING MEDICINE

STRONGER IMMUNE CELLS. SAFER TARGETING. REDUCED MANUFACTURING COST AND COMPLEXITY

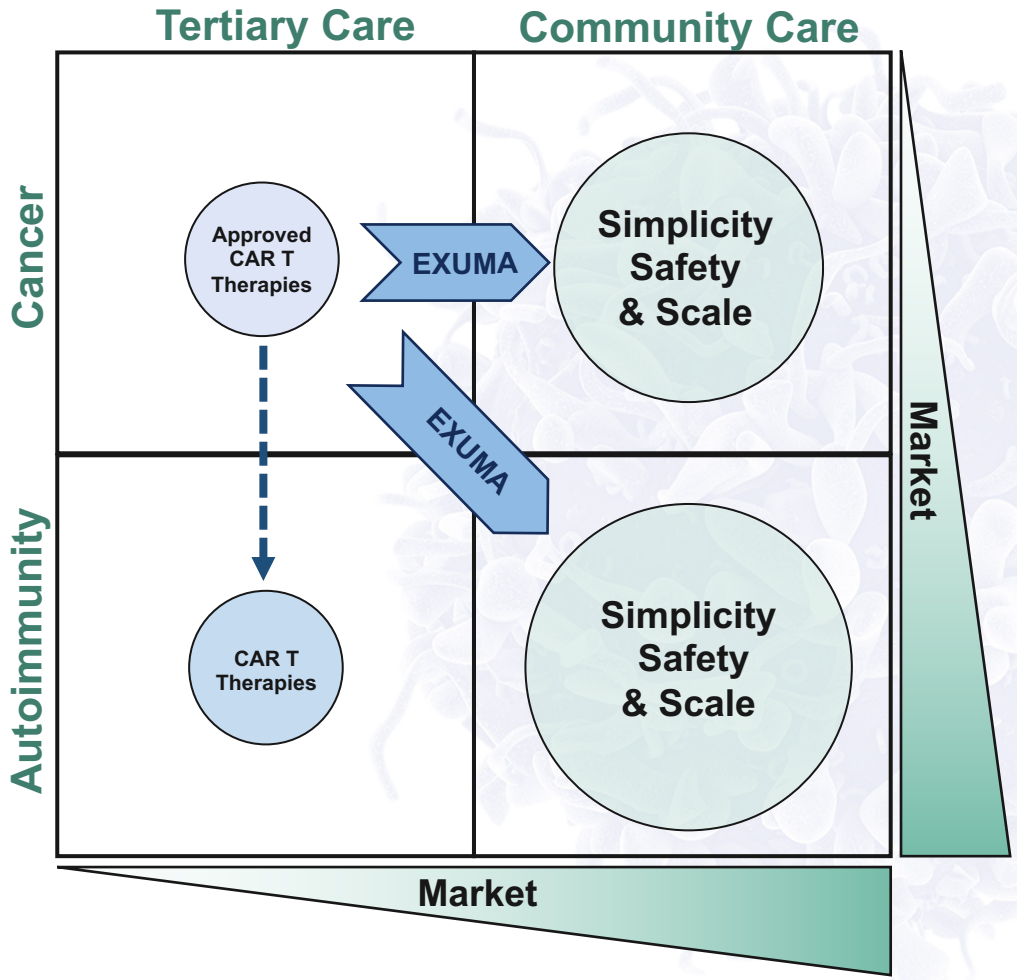
EXUMA BIOTECH – INNOVATING AUTOLOGOUS CELL THERAPY

MISSION: Discover new biology and develop vector delivery solutions to expand and improve patient access to innovative cell and gene therapies

METRICS: Efficacy, Safety and Manufacturing Cost & Complexity

- **EFFICACY:** Optimize effector cell function and exposure (proliferation/persistence) for potency
- **SAFETY:** Enabling cytokine independent, CAR dependent CAR-T cell proliferation and persistence to eliminate chemotherapy, CRS and ICANS
- **MANUFACTURING:** Highly scalable novel gene vector manufacturing technology

The challenges we set out to address 8 years ago are of increased importance for the treatment of autoimmune disease with autologous cell therapy



EXUMA Biotech

EXUMA's Technologies are Built to Overcome the Limitations of Cell Therapy

CD3-DIRECTED LV

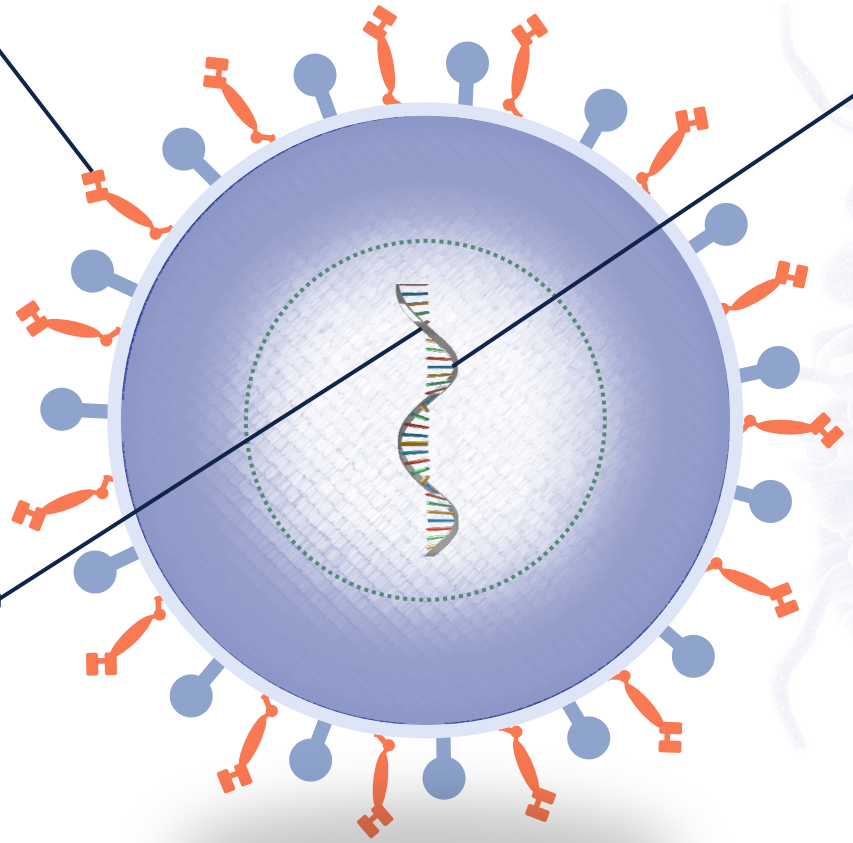
EXUMA's CD3-directed lentivector rapidly targets and loads lymphocytes *ex vivo* or *in vivo* for transduction and proliferation in the patient

- **Reduced manufacturing time, cost & complexity**

FITNESS DRIVER

EXUMA's FITNESS DRIVER transgene encodes a semi-synthetic protein identified for optimization of effector cell stemness, proliferation, persistence, and cytotoxicity without the need for lymphodepleting chemotherapy

- **Enhanced efficacy & safety**
- **Expanded setting of care**



SAFETY SWITCH

EXUMA's safety switch transgene encodes an extracellular target on the transduced cell to permit its removal via antibody infusion

- **Enhanced safety**

Synthetic CAR Ligand (SCL)

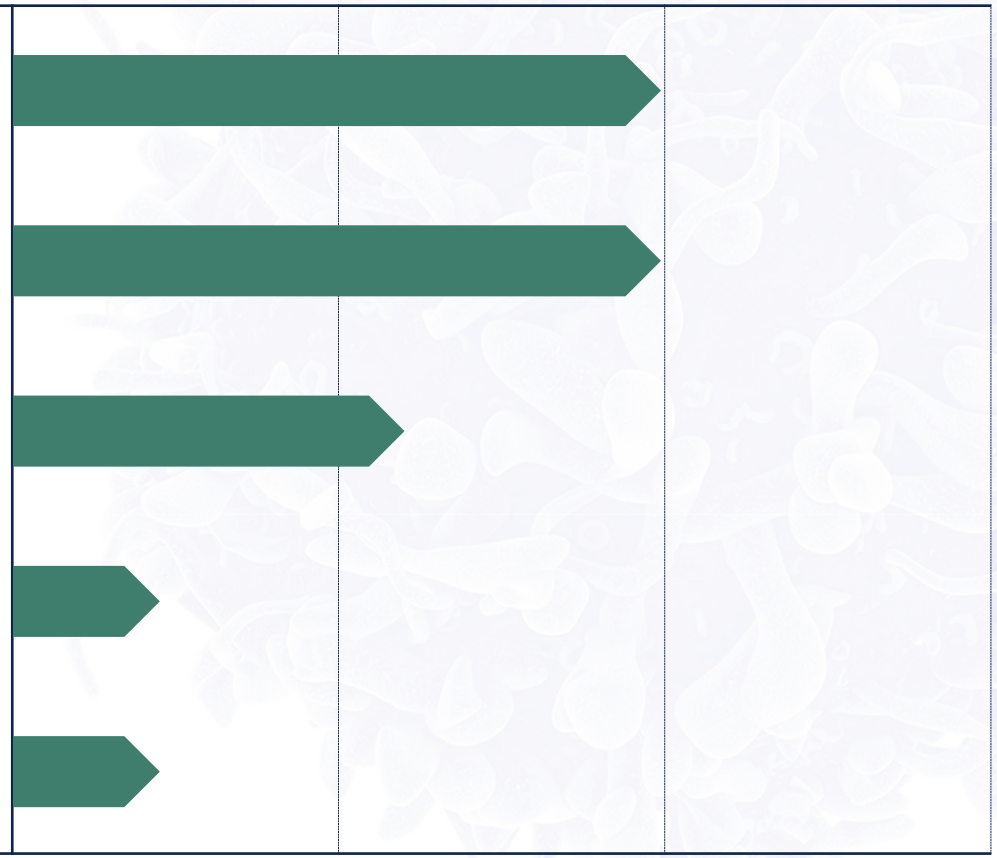
EXUMA's Synthetic CAR ligand enables expansion and persistence with administration of an off-the-shelf mRNA encoding a CAR activating ligand

- **Provides physician control of PK**
- **Enhanced expansion & persistence**

EXUMA Biotech

PIPELINE

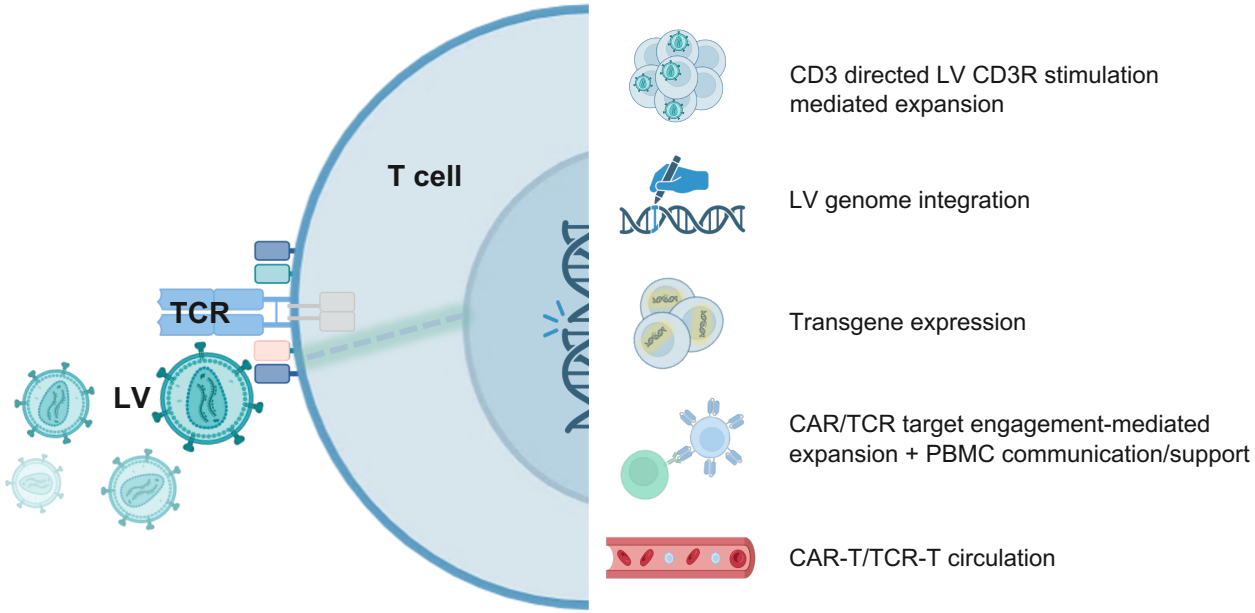
PRODUCT	PLATFORM/ TECHNOLOGY	PATIENT POPULATION	TARGET
CCT303-406	CCT3 + TMR	HER2+ cancers	HER2
CCT301-038	CCT3 + TMR	Osteo & soft tissue sarcomas	AXL
CCT401-752	rPOC	B cell lymphoma	CD19
GCAR product	GCAR	Undisclosed	Undisclosed
mRNA CAR Vaccine	SCL	CAR-T patients	CAR-T cells



EXUMA Biotech

CD3-Targeted Lentivector Technology

Rapid loading of lymphocytes ex vivo or in vivo for all in vivo expansion



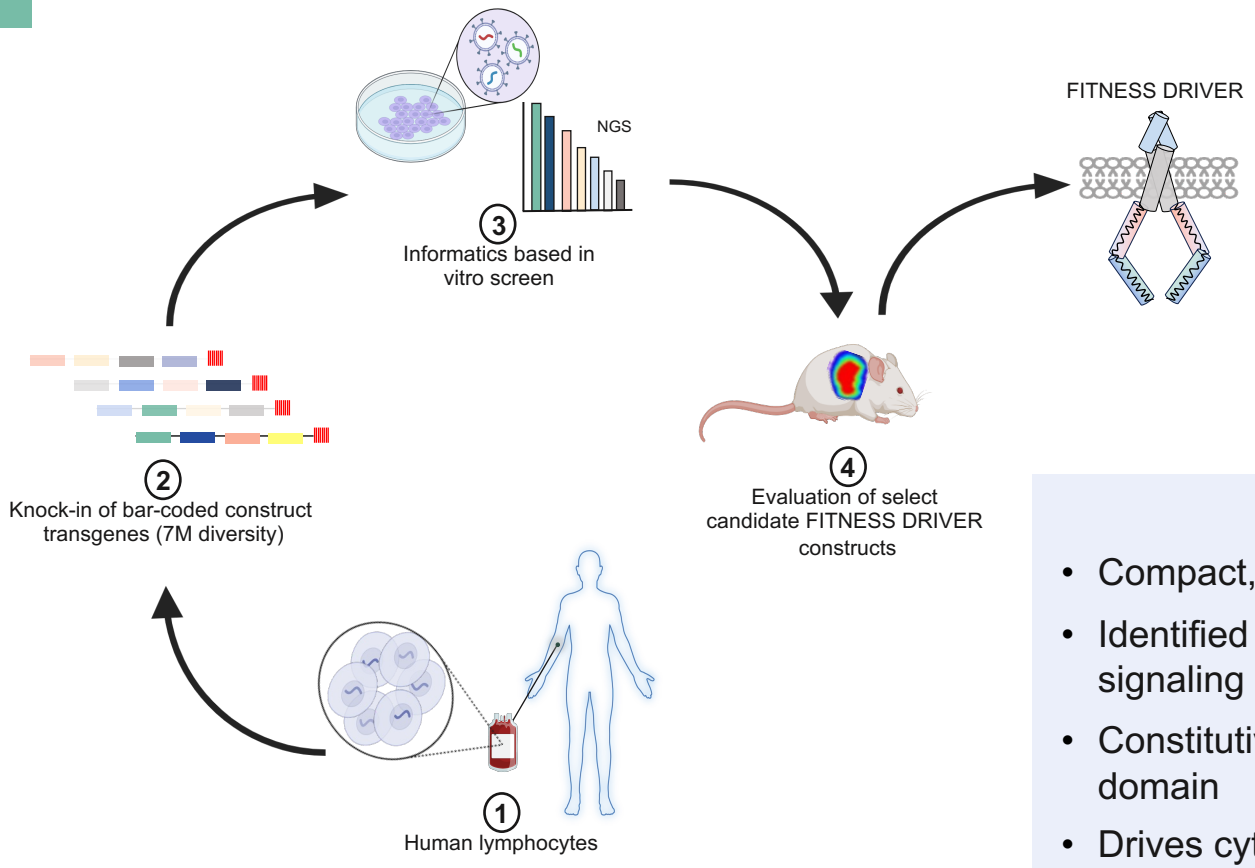
CD3-Targeted LV

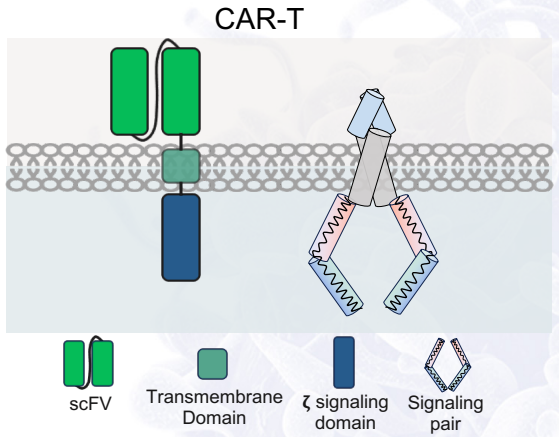
- CD3-targeted lentivector binds, activates and enters (loads) CD3+ lymphocytes
  - No T cell purification
  - Short 4-hour incubation to load lymphocytes
  - No *ex vivo* culture/expansion (preserving T cell stemness)
  - Lower commercial manufacturing cost/complexity
- LV T cell interaction provides the initial stimulus for an ~100-fold expansion of the CAR-T cells *in vivo*, prior to CAR-engagement driven expansion

EXUMA Biotech

FITNESS DRIVER

Identified for optimal CAR-T proliferation, persistence, and cytotoxicity without lymphodepletion



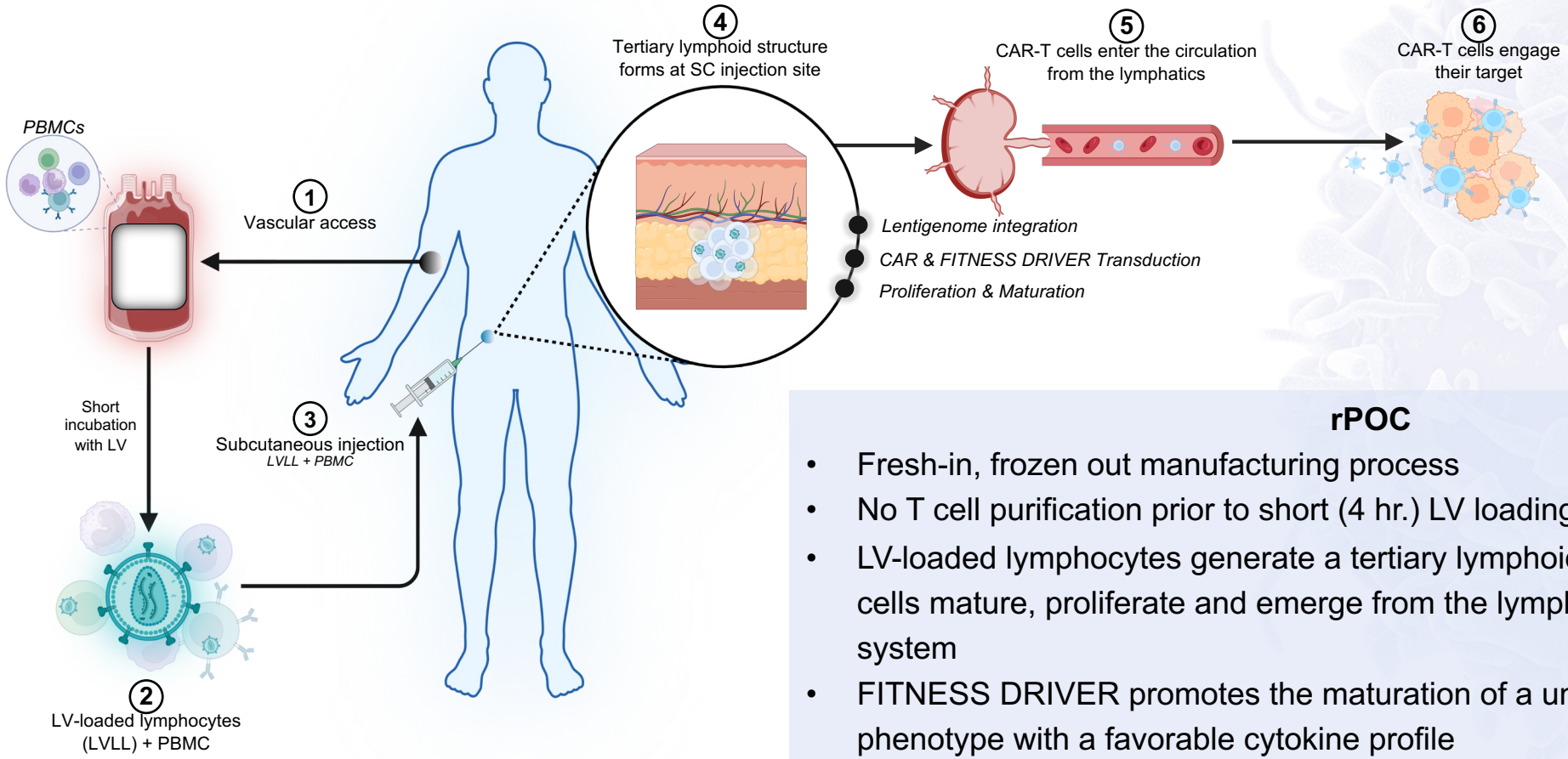


FITNESS DRIVER

- Compact, multi-unit semi-synthetic signaling construct
- Identified from a massively parallel, knock-in, gain of function screen of intracellular signaling domains (native and non-native to T cells)
- Constitutively active FITNESS DRIVER, conditionally active CAR costimulatory domain
- Drives cytokine independent (no lymphodepletion), antigen dependent CAR-T proliferation, persistence and cytotoxicity
- Promotes a unique effector cell phenotype with stem cell memory $T_{SCM}^{CCR7+,\ CD45RA+,\ CD95+}$, $T^{CD8+,\ NKG2D+}$ and NK^{CD56+} features

EXUMA Biotech

rPOC SC – Rapid, Autologous, CAR-T Product for Subcutaneous Injection

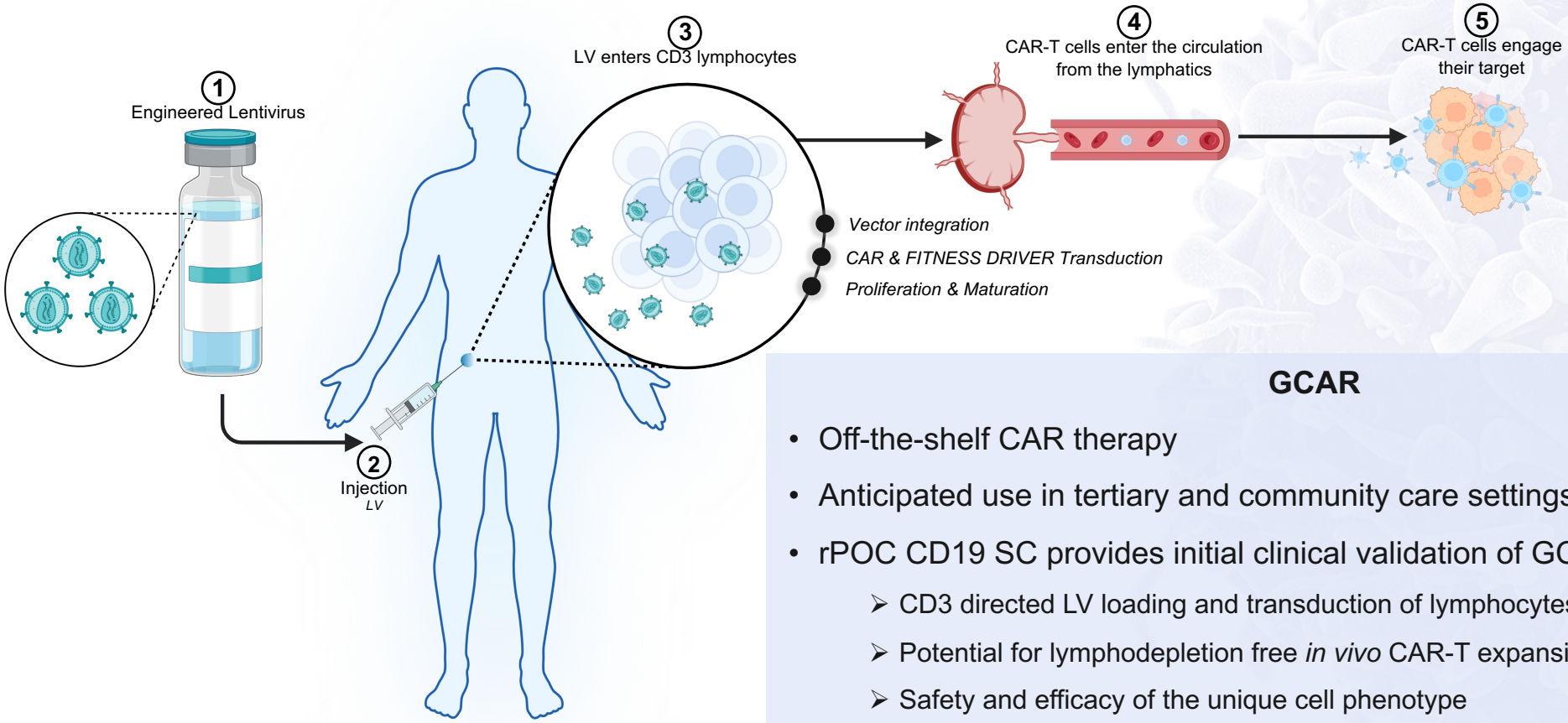


rPOC

- Fresh-in, frozen out manufacturing process
- No T cell purification prior to short (4 hr.) LV loading
- LV-loaded lymphocytes generate a tertiary lymphoid structure where CAR-T cells mature, proliferate and emerge from the lymphatics into the circulatory system
- FITNESS DRIVER promotes the maturation of a unique effector cell phenotype with a favorable cytokine profile

EXUMA Biotech

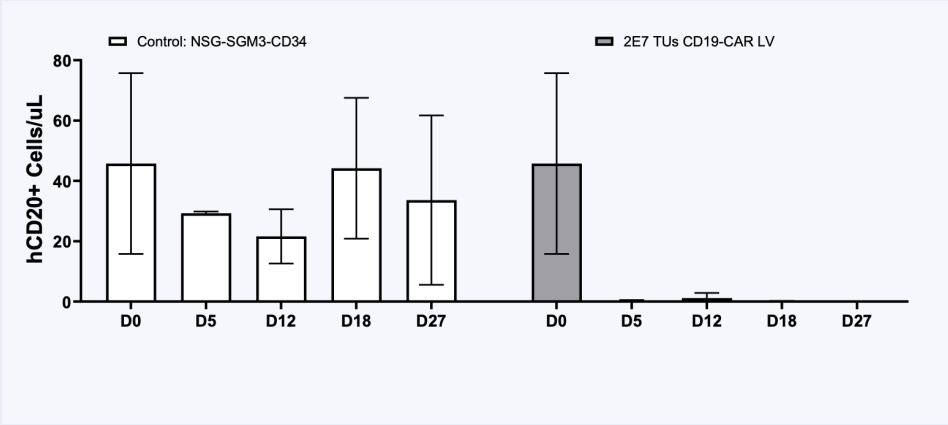
GCAR - CD3-Targeted LV for *In Vivo* Cell Therapy

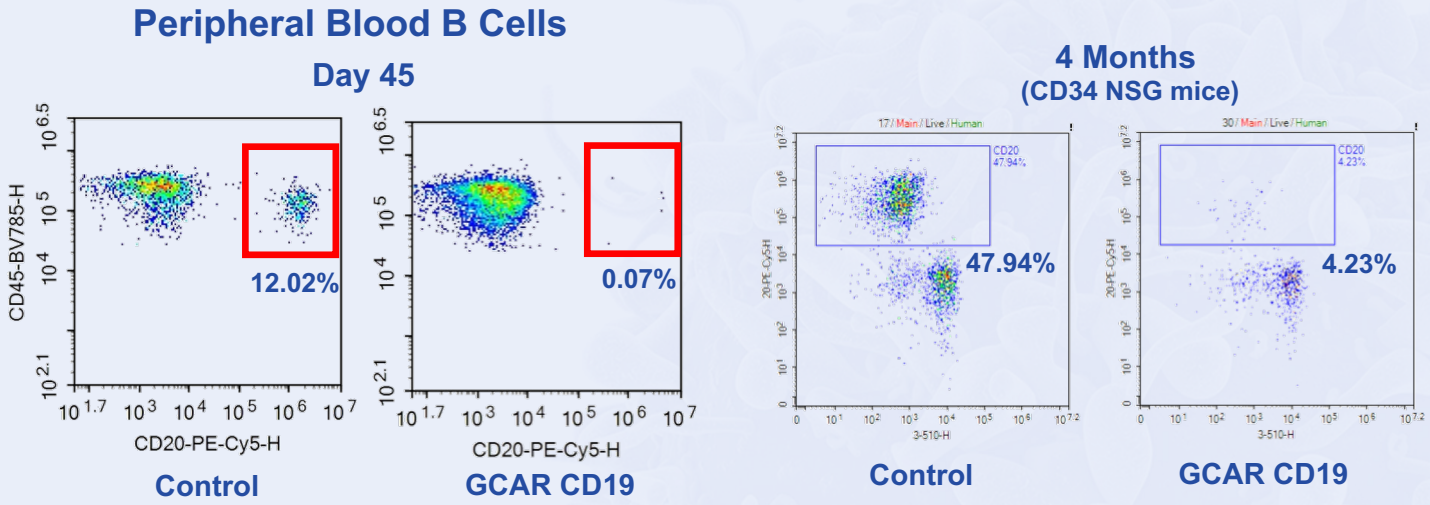


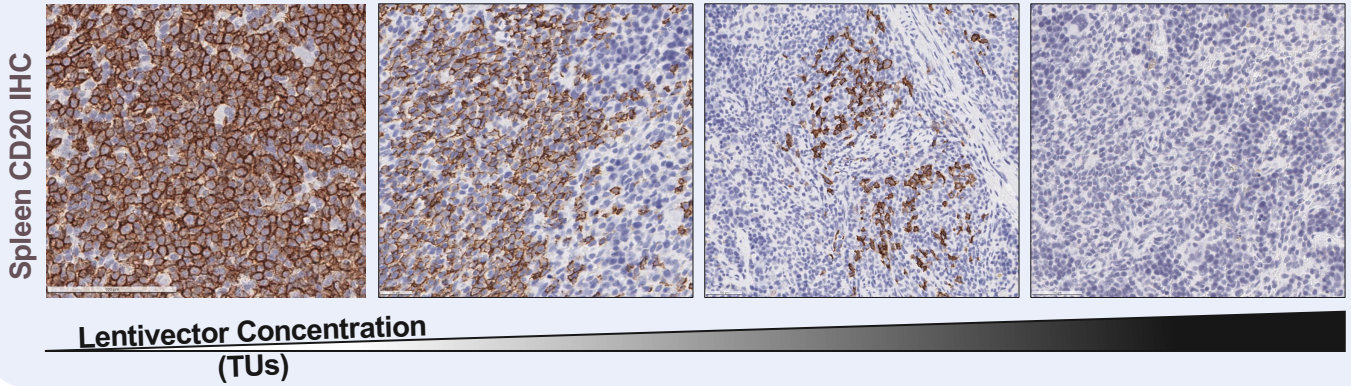
GCAR

- Off-the-shelf CAR therapy
- Anticipated use in tertiary and community care settings
- rPOC CD19 SC provides initial clinical validation of GCAR
  - CD3 directed LV loading and transduction of lymphocytes
  - Potential for lymphodepletion free *in vivo* CAR-T expansion
  - Safety and efficacy of the unique cell phenotype

GCAR-CD19 Causes Rapid, Sustained, Dose-Dependent B Cell Ablation







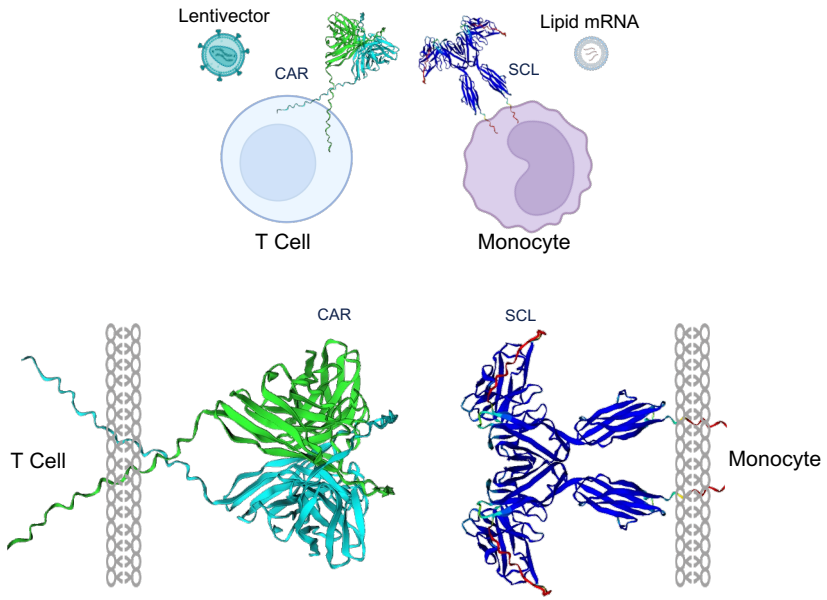
- Intraperitoneal injection of GCAR CD19 lentivector (LV) causes rapid and sustained elimination of B cells in periphery and tissues in multiple mouse models
- GCAR LV dose-dependent elimination of target cells established in SGM3 mice
- Sustained B cell aplasia over 4 months observed in the CD34 NSG mice

EXUMA Biotech

Vigant et al. *AACR 2022, AACR 2023*

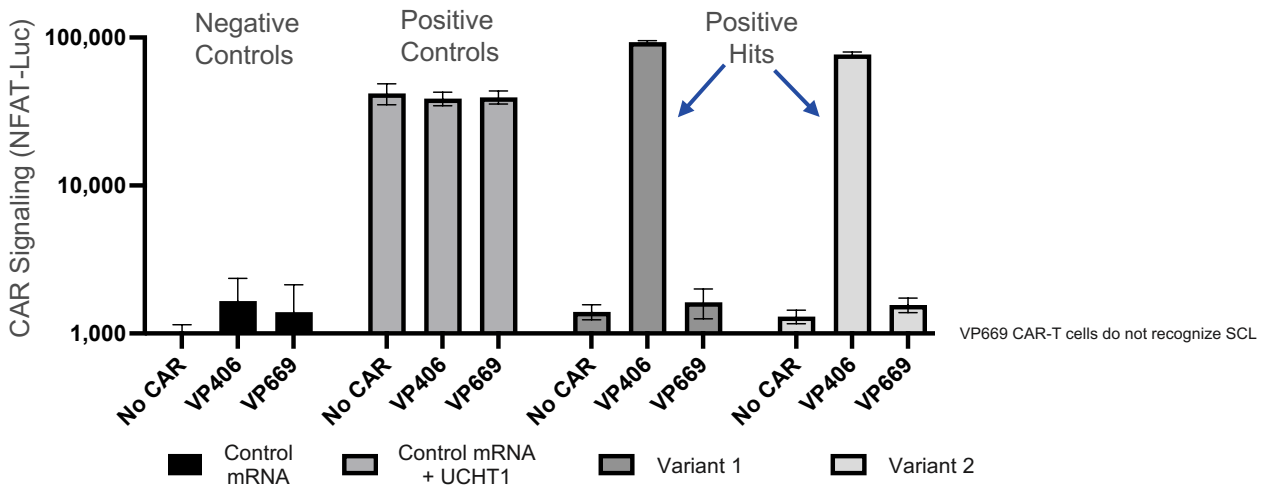
Synthetic CAR Ligand (SCL) – Providing Control of CAR-T PK to the Physician

Simple booster administration could provide long-term CAR-T persistence in treating solid tumors



Multiple mRNA variants encoding synthetic CAR ligand (SCL) construct candidates rapidly synthesized, formulated and screened against EXUMA's TMR HER-2 CAR therapeutic

Synthetic CAR ligands are non-CAR epitope constructs



SCL Technology

- Enables TMR CAR stimulation irrespective of pH
- Dose *in vivo* LNP to increase CAR-T exposure
- Co-deliver in rPOC to drive *in vivo* expansion with lower T cell doses
- Eliminates the cost, complexity, and toxicity of repeated lymphodepletion prior to standard CAR-T

EXUMA Biotech

EXUMA - SUMMARY

- Clinical data from ongoing CD19 rPOC SC program informs potential utility of technology platform for community-based CAR-T therapy in hematologic malignancies and provides an initial foothold for exploration in autoimmune disease
- Clinical validation of rPOC-CD19 without lymphodepletion
  - Represents a potential transformative advance for ACT
  - If CRS/ICANs safety profile confirmed, all barriers to community setting use are eliminated
  - Opens the potential for chemo-free ACT in autoimmune disease settings
  - Provides support for the GCAR *in vivo* approach to provide a true off-the-shelf CAR/TCR-T product

EXUMA Biotech

LIVING MEDICINE

Architects of Cellular Therapy