

# VIRTUAL R&D UPDATE

December 16, 2021

#### FORWARD-LOOKING STATEMENTS

This presentation contains forward-looking statements within the meaning of, and made pursuant to the safe harbour provisions of. The Private Securities Litigation Reform Act of 1995. All statements contained in this document, other than statements of historical facts or statements that relate to present facts or current conditions, including but not limited to, statements regarding possible or assumed future results of operations, business strategies, research and development plans, regulatory activities, market opportunity, competitive position and potential growth opportunities are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause the our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. In some cases, you can identify forward-looking statements by terms such as "may," "might," "will," "should," "expect," "plan," "aim," "seek," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "forecast," "potential" or "continue" or the negative of these terms or other similar expressions. The forward-looking statements in this presentation are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect the our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this presentation and are subject to a number of risks, uncertainties and assumptions, some of which cannot be predicted or quantified and some of which are beyond our control, including, among others: our ability to successfully advance our current and future product candidates through development activities, preclinical studies, and clinical trials; our reliance on the maintenance on certain key collaborative relationships for the manufacturing and development of our product candidates; the timing, scope and likelihood of regulatory filings and approvals, including final regulatory approval of our product candidates; the impact of the COVID-19 pandemic on our business and operations; the performance of third parties in connection with the development of our product candidates, including third parties conducting our future clinical trials as well as third-party suppliers and manufacturers; our ability to successfully commercialize our product candidates and develop sales and marketing capabilities, if our product candidates are approved; and our ability to maintain and successfully enforce adequate intellectual property protection. These and other risks and uncertainties are described more fully in the "Risk Factors" section of our most recent filings with the Securities and Exchange Commission and available at www.sec.gov. You should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in the our forward-looking statements may not be achieved or occur, and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in a dynamic industry and economy. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties that we may face. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.



#### AGENDA

iPSC Cell Therapy Platform and Strategy Lalo Flores, PhD, CEO

**CNTY-101 Update** Hy Levitsky, MD, President of R&D

#### **Treatment Paradigms and Unmet Need in B-Cell Malignancies**

Eduardo Sotomayor, MD, Director of Cancer Institute at Tampa General Hospital

ELiPSE-1: CNTY-101 Phase 1 Trial

Nick Trede, MD, PhD, VP Early Clinical Development

**Century iT Platform Update** 

Luis Borges, PhD, CSO

#### Q&A

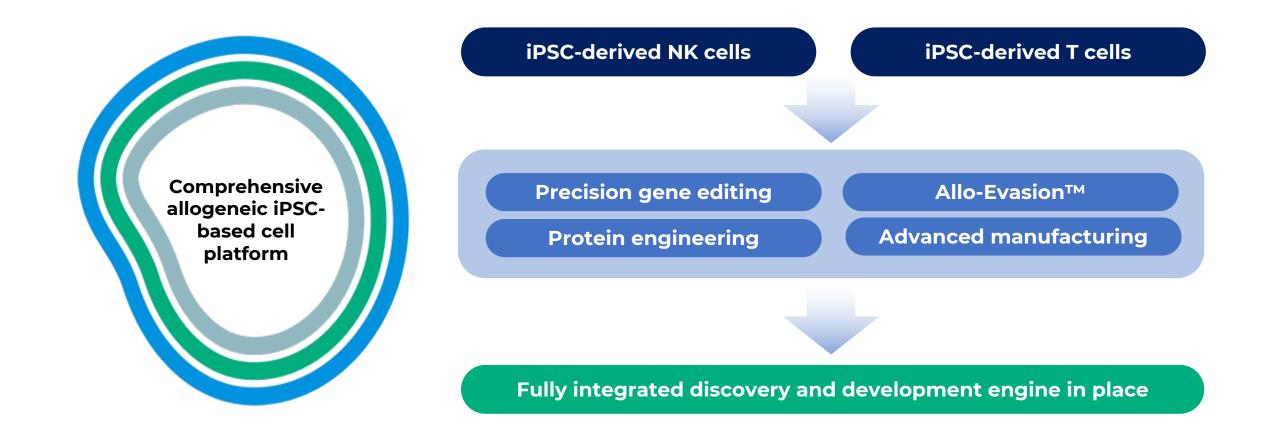


# IPSC CELL THERAPY PLATFORM AND STRATEGY

Lalo Flores | CEO

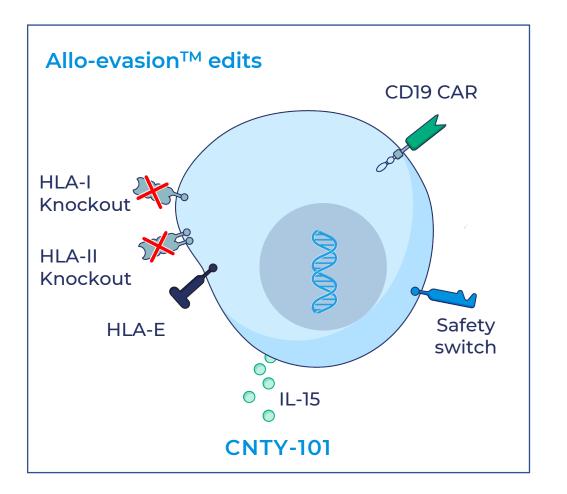


#### **CENTURY'S NEXT GENERATION IPSC TECHNOLOGY PLATFORM**





### **CENTURY'S DIFFERENTIATED STRATEGY**



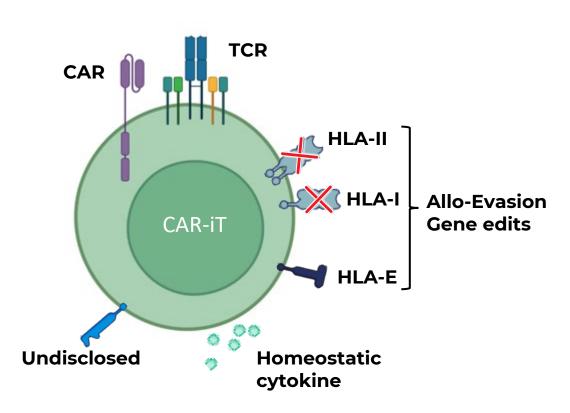
#### CNTY-101

- CD19 targeted iNK product with best-in-class potential
  - First cell product candidate with 6 gene edits introduced with CRISPR-HDR
  - Incorporates Allo-evasion gene edits designed to potentially prevent allorejection and enable higher drug exposure after multiple doses
- ELiPSE-1 Phase 1 study designed to maximize learnings



### **CENTURY'S IPSC-DERIVED CAR-T PLATFORM (CAR-IT)**

- Preclinical data supports decision to prioritize  $\gamma\delta$  iT platform for first CAR-iT products
- γδ iT cells have potential for enhanced expansion and trafficking to non-hematopoietic compartments
  - Preferred choice for solid tumor pipeline
- CNTY-102 will be Century's first  $\gamma \delta$  iT product
  - Potential to combine with CNTY-101 to address unmet need in all types of B-cell malignancies



 $\gamma \delta$  iT Platform



Product	iPSC Platform	Targets	Indications	Ownership	Expected IND Submission	Discovery Preclinical Phase 1 Phase 2	Phase 3
CNTY- 101	iNK	CD19	<b>B-Cell Malignancies</b>	CENTURY	Mid 2022		
CNTY- 103	iNK	CD133 + EGFR	Glioblastoma	CENTURY	2023		
CNTY- 102	iT	CD19 + CD79b	<b>B-Cell Malignancies</b>	CENTURY	2024		
CNTY- 104	iNK	Multi- specific	Acute Myeloid Leukemia		2024		

Solid Tumors Hematologic Tumors



#### ANTICIPATED 2022 R&D CATALYSTS

Pipeline	<ul> <li>CNTY-101: IND filing and Phase 1 start</li> <li>CNTY-103: Initiation of IND enabling activities</li> <li>Future pipeline candidates</li> </ul>
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Platform	<ul> <li>Disclosing multiple updates at medical and scientific congresses throughout 2022</li> </ul>
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# **CNTY-101 UPDATE**

Hy Levitsky, MD | President of R&D



#### Distinct Biology of NK cells vs T cells Influence on Platform Development

NK vs T CELL BIOLOGY				
Proliferative capacity	T cell >> NK cell			
Persistence/memory	T cell >> NK cell			
Pharmacokinetics	Cmax and AUC after single dose: T cells > NK cells			
Trafficking	NK cell: lympho-hematopoietic compartment T cell: all tissues			
<ul><li>Toxicity Risks</li><li>GVHD</li><li>CRS/neurotoxicity</li><li>On target toxicity</li></ul>	<ul> <li>GVHD: T cell &gt; NK cell (can be mitigated by editing)</li> <li>CRS/neurotoxicity: T cell &gt; NK cell</li> <li>On target/off tumor toxicity: T cell &gt; NK cell (persistence)</li> </ul>			



# NK CELL-BASED THERAPIES SHOW PROMISING EARLY SIGNALS OF SAFETY AND EFFICACY IN R/R NHL

	iC9/CAR.19/IL15 -Transduced CB-NK	GDA-201	FT516	FT5	96
Regimen	-	+ IL-2 + rituximab	+ anti-CD20 mAb + IL-2	Monotherapy	+ anti-CD20 mAb
CR, %	67%	65%	44%*	30%*	56%*
CRS, all G (G≥3)	No CRS	No CRS	No CRS	8% G1	11% G1-2
NE, all G (G≥3)			No ICANS		
*≥ 90M cells					

- Even in dose escalation, response rates are clinically meaningful
- Good safety profile
- Durability and impact of re-dosing to be determined



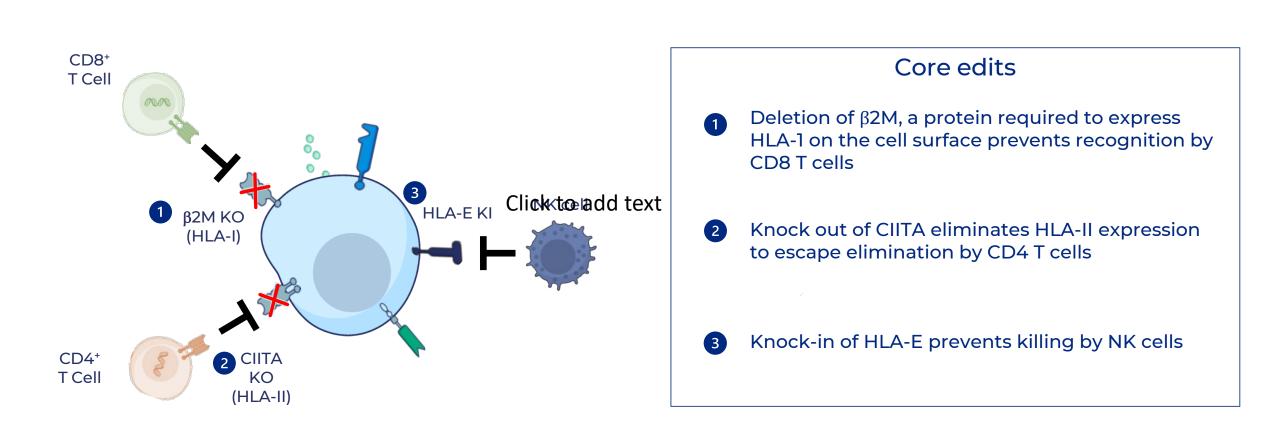
#### POTENTIAL ADVANTAGES OF REDOSING

- Experience with autologous CAR-T established the impact of "drug exposure" (PK AUC) on disease response
- Repeat dosing of CAR-iNK cells can extend drug exposure to achieve potentially deeper and more durable remissions
- Infusion of fresh cells may mitigate cell exhaustion that limits single dose strategies
- Off the shelf availability of iPSC derived products enables a cyclical treatment paradigm common with most other forms of cancer therapy

But only if initial dosing does not prime an allo-rejection response!

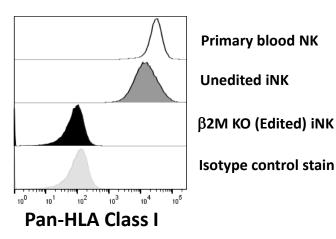


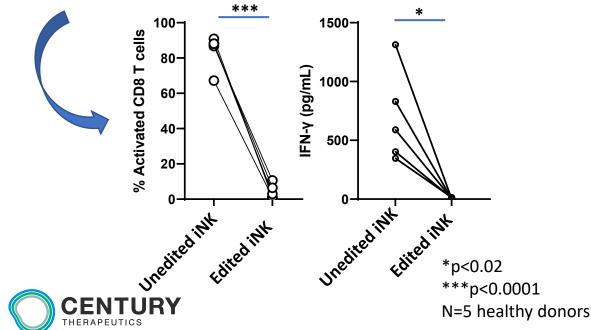
#### ALLO-EVASION<sup>™</sup> 1.0 DESIGNED TO OVERCOME 3 MAJOR PATHWAYS OF HOST VS GRAFT REJECTION

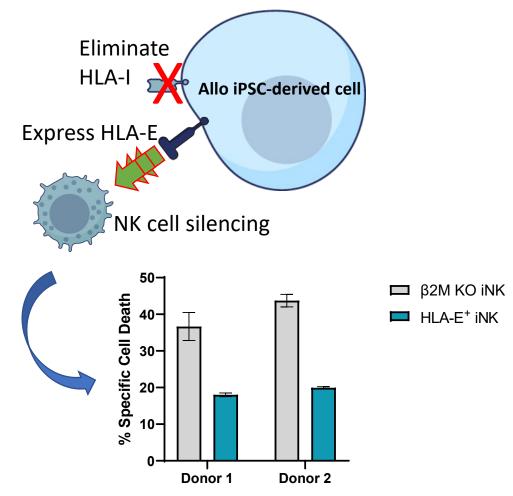




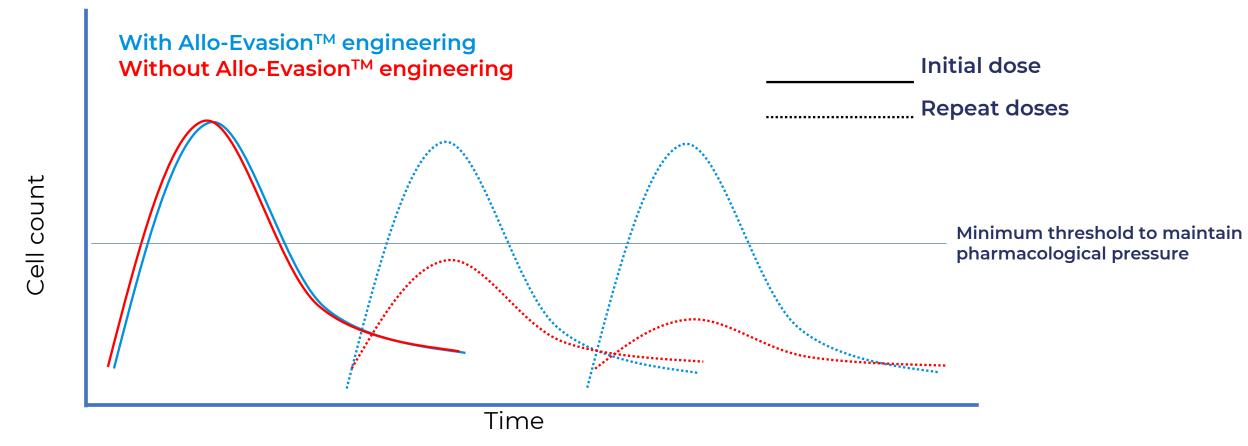
#### ALLO-EVASION<sup>™</sup> 1.0 EDITS RENDER CELLS RESISTANT TO T CELL AND NK CELL KILLING





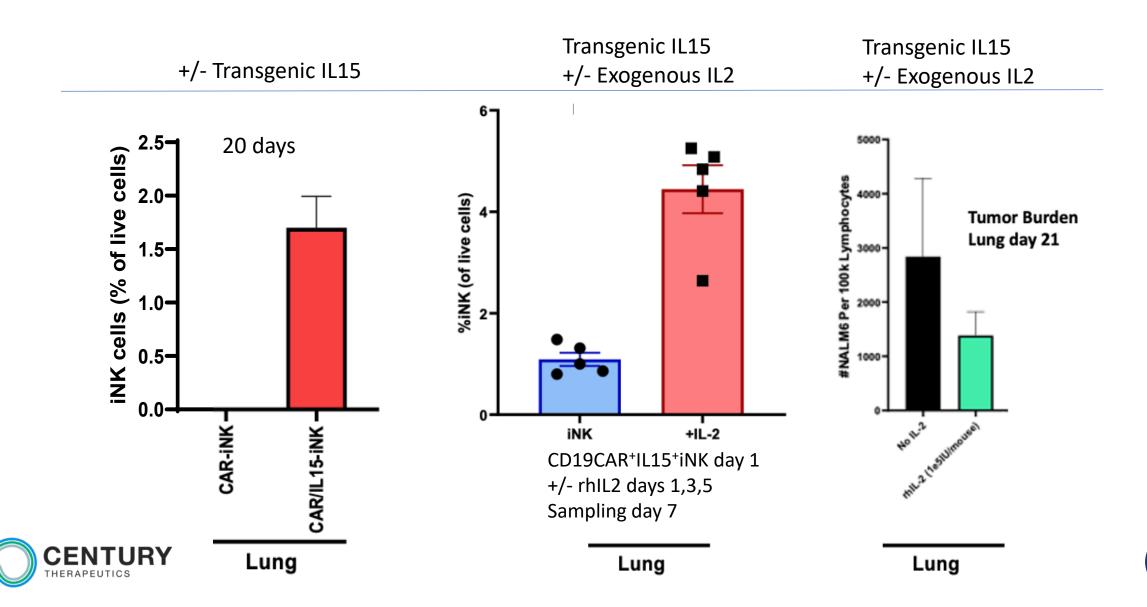


# ILLUSTRATIVE POTENTIAL OF ALLO-EVASION<sup>™</sup> ON CELLULAR PHARMACOKINETICS AND REPEAT DOSING

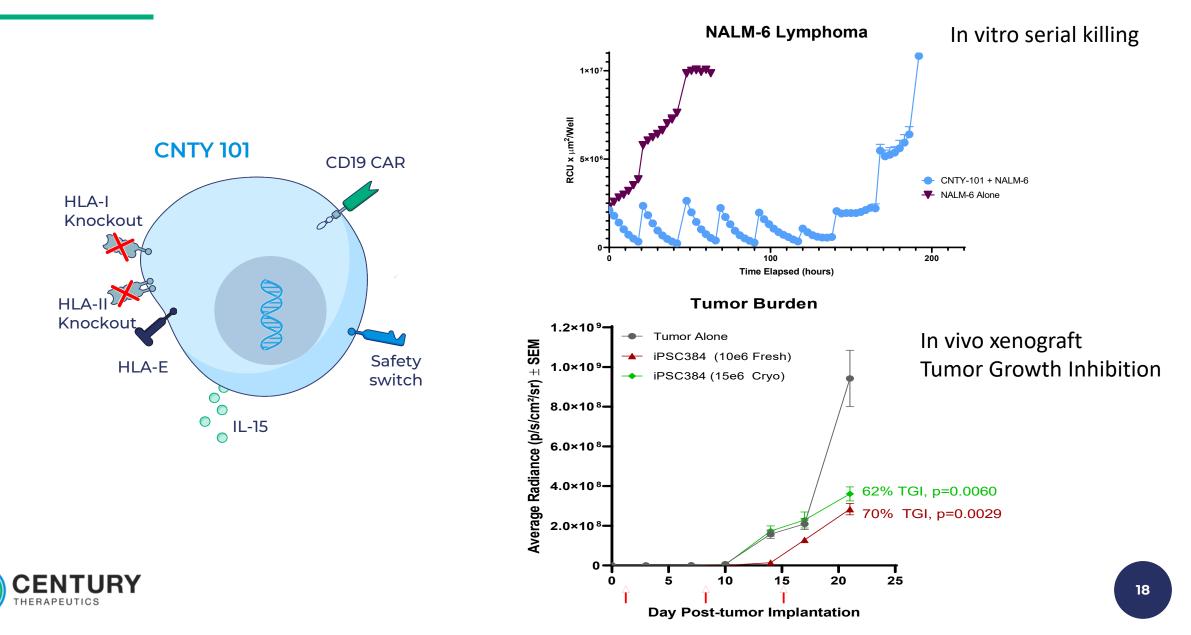




#### INTRINSIC IL15 AND EXTRINSIC IL2 IMPROVE CAR-INK PERSISTENCE AND TUMOR CLEARANCE IN TISSUES (LUNG)



# CNTY-101 DEMONSTRATES ROBUST TUMOR KILLING IN VITRO AND IN VIVO





- CNTY 101 is Century's first iPSC-derived NK cell therapy candidate for the treatment of CD19+ B cell malignancies
- Incorporates a comprehensive gene editing strategy to evade CD4<sup>+</sup> and CD8<sup>+</sup> T cell and NK cell mediated allo-rejection and have potentially favorable pharmacokinetics
- Product candidate designed to enable repeat dosing, potentially achieving greater drug exposure and deeper and more durable clinical responses
- IND filing on track for mid 2022





Treatment Landscape of Non-Hodgkin's Lymphomas: It seems to be a crowded field...but it depends how you see it and/or approach it....







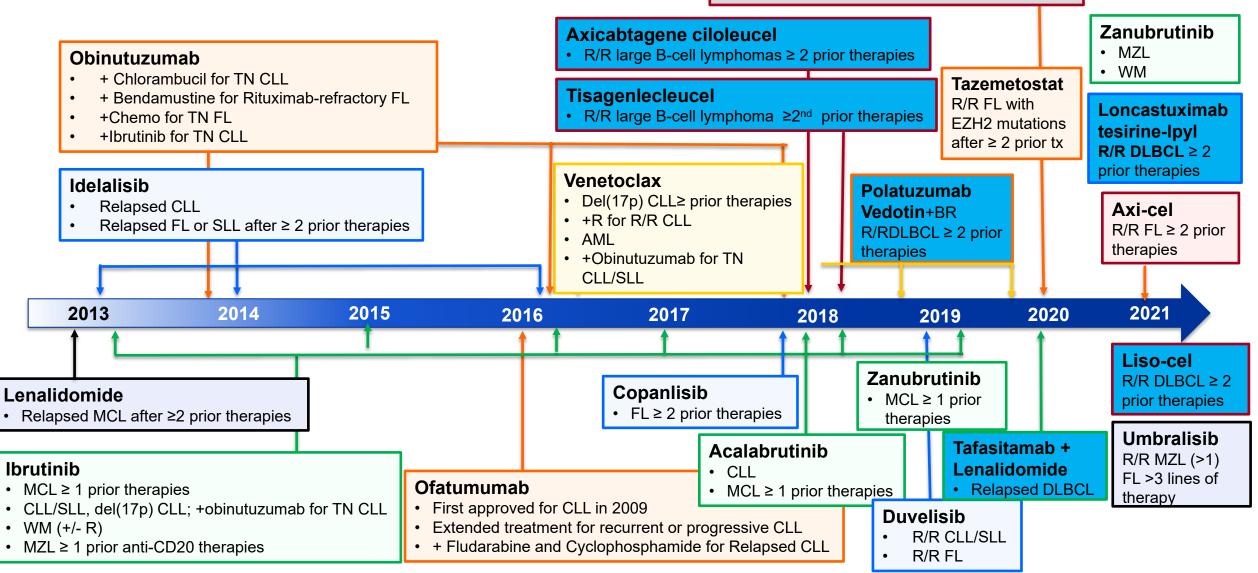
#### Eduardo M. Sotomayor, MD

Director, TGH Cancer Institute Professor, Morsani College of Medicine University of South Florida

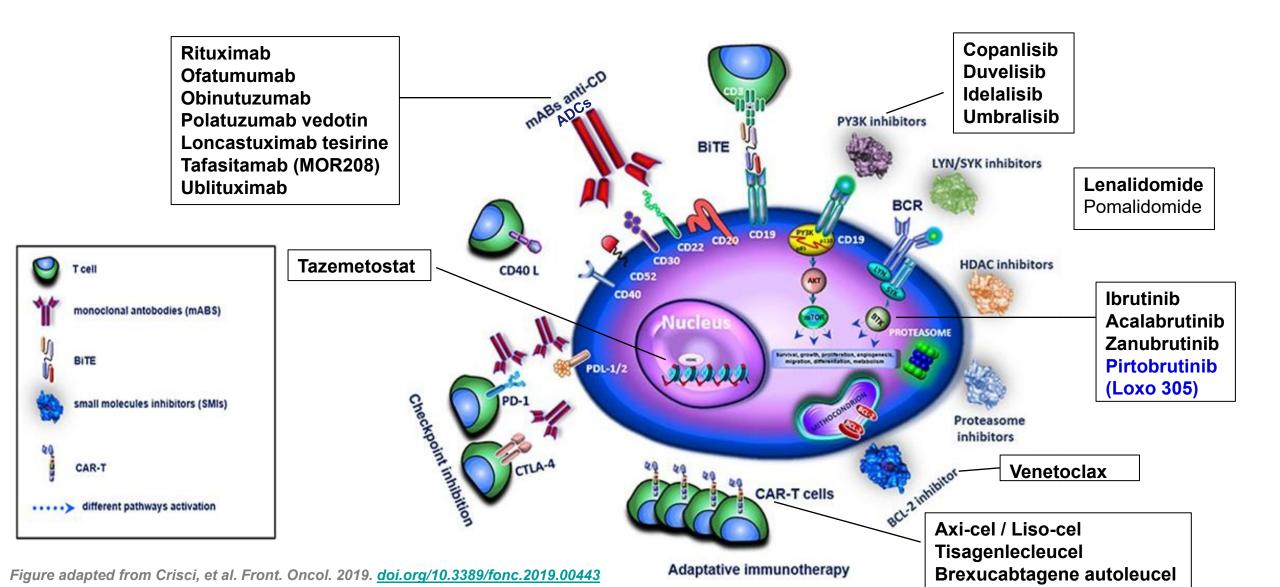
# **Timeline of Newer Agents for B-cell NHL**

Brexucabtagene autoleucel





### **Targeted Therapy and Immunotherapy of B-cell NHL**



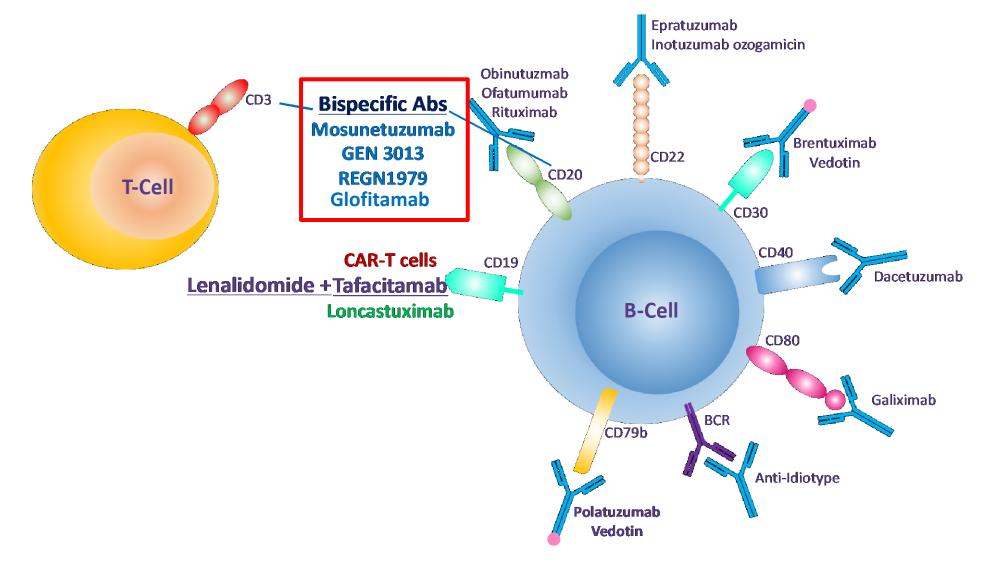
# Immunotherapy: Targeting CD19 and CD20 (Again...)

- **CD19** is an enticing target for novel approaches:
  - Tafasitamab, anti-CD19 antibody (+/- Lenalidomide)
  - Loncastuximab Tesirine (Anti-CD19 Antibody-Drug Conjugate)
- CD20 is....again an enticing target for bi-specific antibodies:
  - Several bi-specific directed T-cell engager (BITE) targeting CD20 and CD3 (CD20 x CD3)....
- CD79b targeted ADC
  - Does Polatuzumab vedotin change standard of care?

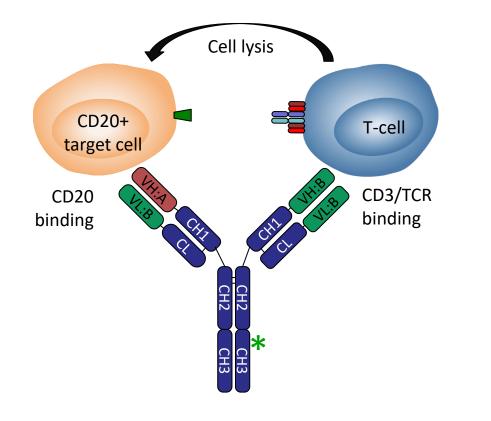
#### Immunotherapy: Lessons learned from failures... Checkpoint blockade.....perhaps setting is critical

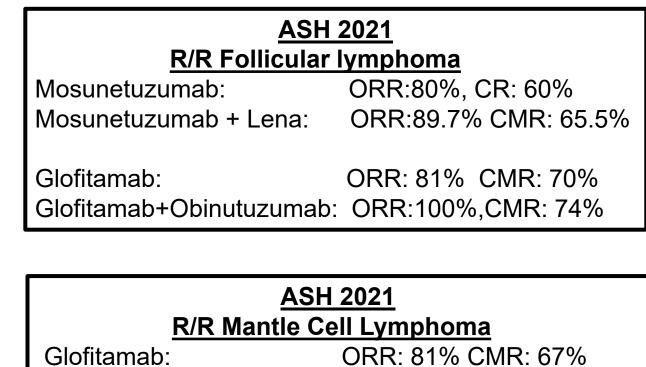
- Unlike the success in Hodgkin's lymphoma, clinical trials with checkpoint blockade antibodies in relapsed/refractory B-cell NHL have been disappointing so far:
  - Despite malignant B-cells being surrounded by an "army" of T-cells
  - Role of the immunosuppressive Tumor Microenvironment (TME). TME is prognostic and potentially predictive of outcomes in DLBCL<sup>1</sup>
- Perhaps frontline (different setting) checkpoint inhibition, given when host immunity is relatively intact, might improve outcomes in DLBCL
  - Indeed, it has been shown in the neoadjuvant setting for several solid malignancies...including responses in subtypes not known to be sensitive to checkpoint blockade
- Anti-PDL1 (Avelumab) + Rituximab x 2 cycles in DLBCL (Hawkes, E. et al 2020)
  - ORR of 60% with a CR of 21% suggest potential synergy and superior efficacy of PDL1 inhibition in the frontline setting as compared to prior studies in the R/R setting. Patients then went to receive standard R-CHOP with achievement of a CR of 89%

## ASH 2021....the saga continues: Bispecific Antibodies



#### <u>"Game changer": Bispecific antibodies</u> <u>Human anti-CD20 x anti-CD3 Monoclonal Bispecific Antibody</u>





Cross-linking results in targeted activation of local T-cells and T-cell-mediated killing of CD20+ B-cells (independently of TCR-mediated recognition)

# **Bi-Specific Antibodies: Safety**

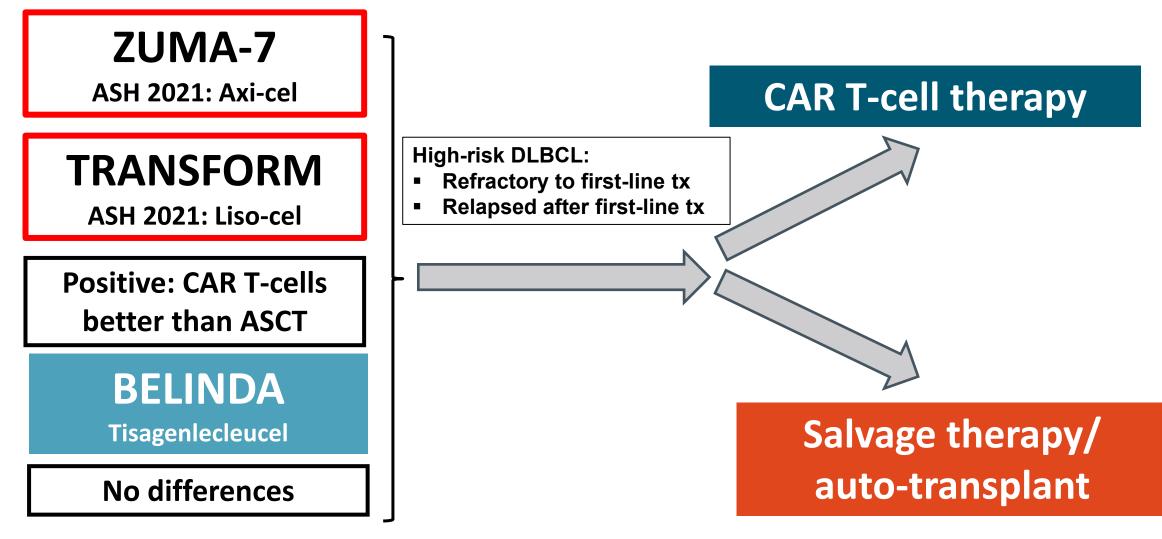
Antibody	Glofitamab	Mosunetuzumab	Odronextamab	Epcoritamab
Ν	64 ( > 600 ug)	131	136	58
CRS any CRS <u>&gt;</u> 3	63.5% 3.8%	28.9% 1.1%	61% 7.3%	59% 0
NT any NT <u>&gt;</u> 3	43.3% NR	49% 1.1%	NR 3.6%%	6.9% 3.4%

CRS, cytokine release syndrome; NT, neurotoxicity

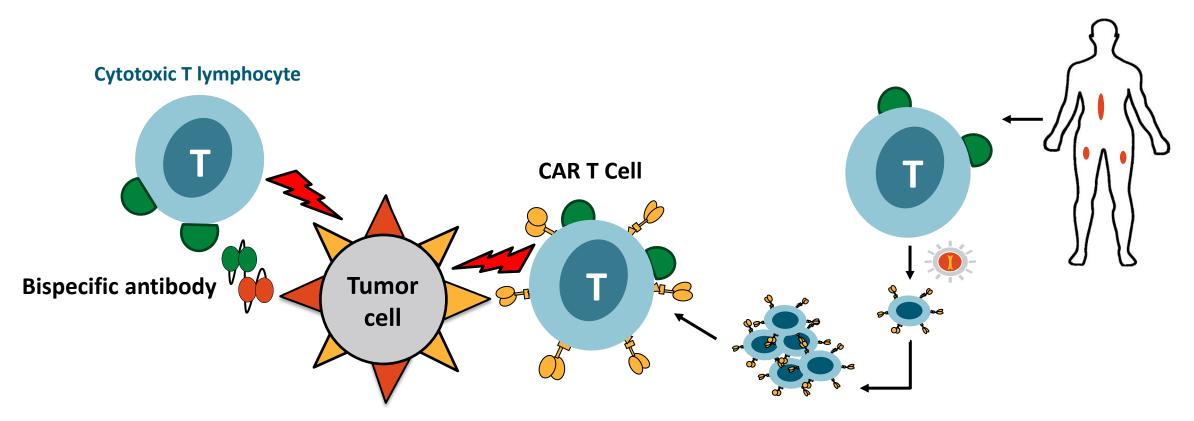
## Immunotherapy: Targeting CD19 in B-cell lymphomas Successes, Failures and Opportunities

- Autologous CD19 CAR T-cells have shown significant efficacy in patients with relapsed/refractory CD19 positive DLBCL and other B-cell lymphomas.
  - Three platforms are FDA-approved (Axi-cel, Tisa-cel and Liso-cel) for DLBCL
  - One platform approved for MCL (Brexucabtagene autoleucel)
  - One platform approved for follicular lymphomas (Axi-cel)
  - Cost, manufacture time, toxicity, progression while waiting for engineered T cells. Mechanisms of resistance
  - It is estimated that 30-40 percent of patients with large B-cell lymphoma might be cured with CD19 CAR T-cells....
  - Remaining 60 percent: Unmet need
- Moving CD19 CAR T cells into the first relapse setting:
  - Is it better than autologous stem cell transplant for patients with DLBCL that relapsed within 12 months of frontline chemoimmunotherapy?
  - ASH 2021: ZUMA-7, TRANSFORM and BELINDA Trials

# ASH 2021: Will CD19 CAR T-cell Replace Autologous transplant for DLBCL?



### **Bispecific Antibodies vs. Autologous CAR T-Cells**



Characteristic	Bispecific Antibodies	CAR T-Cell Therapy
Preparation	"Off the shelf"	In vitro manufacturing (3-4 wks)
Dosing	Repetitive	Single (following lymphodepleting CT)
CRS incidence	Less	Greater

# **Targeted Therapy: Many successes...but also limitations**

- Novel targeted agents either alone or in combination are improving clinical outcomes of patients with B-cell lymphomas, mainly in the *relapsed/refractory* setting
- Some of them have been (or are being) evaluated as *frontline therapy* alone or in combination in some B-cell malignancies (CLL/SLL; MCL)
- Overall, improvement in PFS, minimal impact in OS
- Many patients either do not respond to targeted agents *(innate resistance)* or, after an initial response they progress *(acquired resistance)*.
- Room for additional targeted therapies......

# <u>Unmet needs + Good Science = Opportunities in a</u> <u>"crowded" Therapeutic Landscape</u>

#### I. <u>Good Science</u>:

- Beyond T-cell immunotherapies... Harnessing Innate Immunity
  - Genetically engineered NK cells
    - Genetically engineered Macrophages

## II. Unmet Needs in Non-Hodgkin's lymphomas

- Difficult to treat lymphomas:
  - Double/triple hit large B cell lymphomas
  - POD24 low grade lymphomas
  - MCL with p53 abnormalities
  - Transformed lymphomas
  - Primary CNS lymphomas
  - Viral-associated lymphomas

# <u>Unmet needs + Good Science = Opportunities in a</u> <u>"crowded" Therapeutic Landscape</u>

### II. Emerging Needs in Non-Hodgkin's lymphomas

- Innate or acquired resistance to novel agents
  - BTK resistance (MCL, CLL, WM, MZL)
  - CD19 CAR T-cells (DLBCL, MCL, FL).... CLL
  - Double refractory (FL, MCL)

### III. "Wide open" lymphomas for.....novel therapies

- T-cell/NK malignancies
- Viral-associated lymphomas
- CNS lymphomas

# ASH 2021:"Off the Shelf" Engineered Cellular Products: Allogeneic Therapies

#### **Advantages**

- Eliminates the manufacturing time and allows true point of care administration
- Expand access to therapy (ie, leukopenic patients)
- Improve safety through genetic manipulation
- Can scale to much larger numbers with broader impact for those in need (not achievable with the generation of an autologous product for each patient)

#### **Requirements**

- Should not induce GvHD
- Should not result in immune rejection of cellular product
- Immediately available
- Precise genetic engineering

Modified from Crooks, G.M. ASH 2020

# **ASH 2021: Sources of Allogeneic Cells**

Healthy Donor	Pluripotent stem cells
Peripheral Blood (T-cells)	<ul> <li>iPSC (inducible pluripotent stem cells)</li> </ul>
Umbilical Cord (NK cells)	• T-iPSC (T)
- Mature cells	
- Multiple products per donation (up to 100 products)	<ul> <li>Self-renewing. Expanded indefinitely Homogenous product available in large batches</li> </ul>
-Non-self renewing	-Complex editing is possible
-Heterogenous starting product makes consistency challenging	-Complex differentiation process is a challenge

# **Conclusions**

- Despite the progress that has been made in the treatment of NHL, there are still several unmet needs
  - Emerging needs as a result of changing treatment landscape
    - ie resistance to targeted/immune based therapies
- Strategies to harness innate immunity represent a compelling opportunity to address these gaps
  - Potential for off-the-shelf engineered cell therapies





## CANCER



### **THANK YOU!**



### esotomayor@tgh.org

## **CNTY-101 PHASE I TRIAL DESIGN**

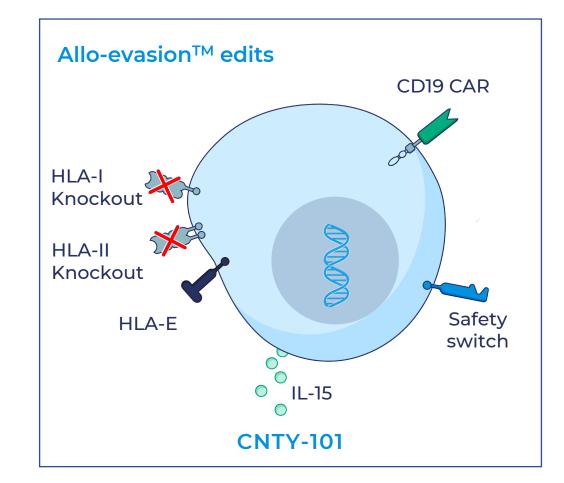
Nick Trede, MD, PhD | VP Early Clinical Development



### CNTY-101: AN ALLOGENEIC, iPSC-DERIVED CAR-INK PRODUCT CANDIDATE TARGETING CD19 FOR R/R B-CELL MALIGNANCIES

### CNTY-101 has the potential to change the lymphoma patient treatment paradigm

- Potentially treat patients immediately upon diagnosis
- Based on Allo-evasion and anticipated ability to give **additional cycles of treatment**, potential to enhance depth and durability of response
- Potential to avoid lymphodepletion with additional treatment cycles due to reduced alloreactivity, and engineered IL-15 to potentially improve the safety profile
- Availability of CNTY-101 off-the-shelf potentially enables outpatient use at any clinical site, improving **patient access**





THE ELIPSE-1 STUDY: A PHASE 1, MULTICENTER, OPEN-LABEL STUDY OF CNTY-101 IN SUBJECTS WITH RELAPSED OR REFRACTORY CD19 POSITIVE B CELL MALIGNANCIES - KEY SELECTION CRITERIA

#### **INCLUSION CRITERIA**

- Aggressive NHL: DLBCL, HGBL, PMBCL MCL, tFL, FL3B
- Indolent NHL: FL, MZL
- <u>At least 2 prior lines</u> of therapy, including anthracycline (or alkylator for iFL) and anti-CD20 antibody
  - Patients who have already undergone or are unable to undergo CAR T therapy are eligible
- ECOG score of 0 or 1
- Adequate organ function
- Willing to undergo required biopsies

### EXCLUSION CRITERIA (cannot meet any)

- CNS-only disease
- Prior allo stem cell transplant
- Recent other malignancies
- Ongoing infections
- Cardiac insufficiency
- CNS pathology
- COVID infection (by PCR test) within 10 days (mild/asymptomatic) or 20 days (severe/critical). Symptoms must have resolved.
- COVID vaccine within 14 days

CENTURY

For outpatient treatment (preferred) patients have to stay within 60 minutes of the site (hotel accommodation will be provided)

### **ELIPSE-1 OBJECTIVES**

#### **Primary**

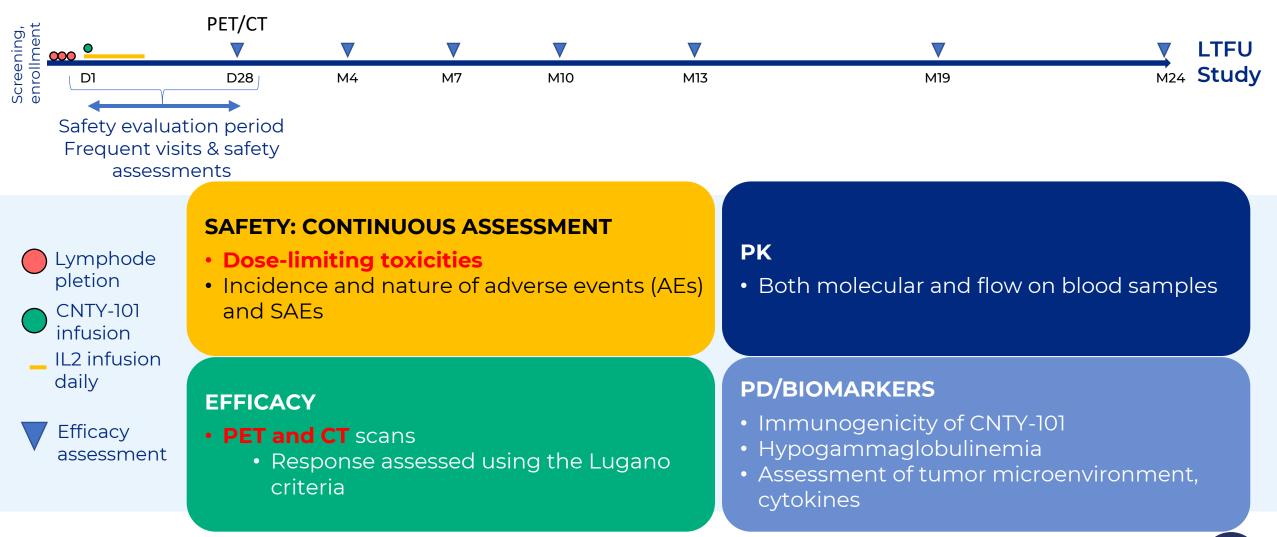
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Maximum-tolerated dose (MTD) or maximum administered dose regimen of CNTY-101
(dose and schedule of CNTY-101 with IL-2)
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Recommended phase 2 regimen (RP2R) of CNTY-101 + IL-2

Secondary	
Antitumor activity	
PK profile	
Safety and tolerability at RP2R	
Time to dosing	
Exploratory	
Feasibility of additional treatment cycles	
PD parameters: immune responses: biomarkers	

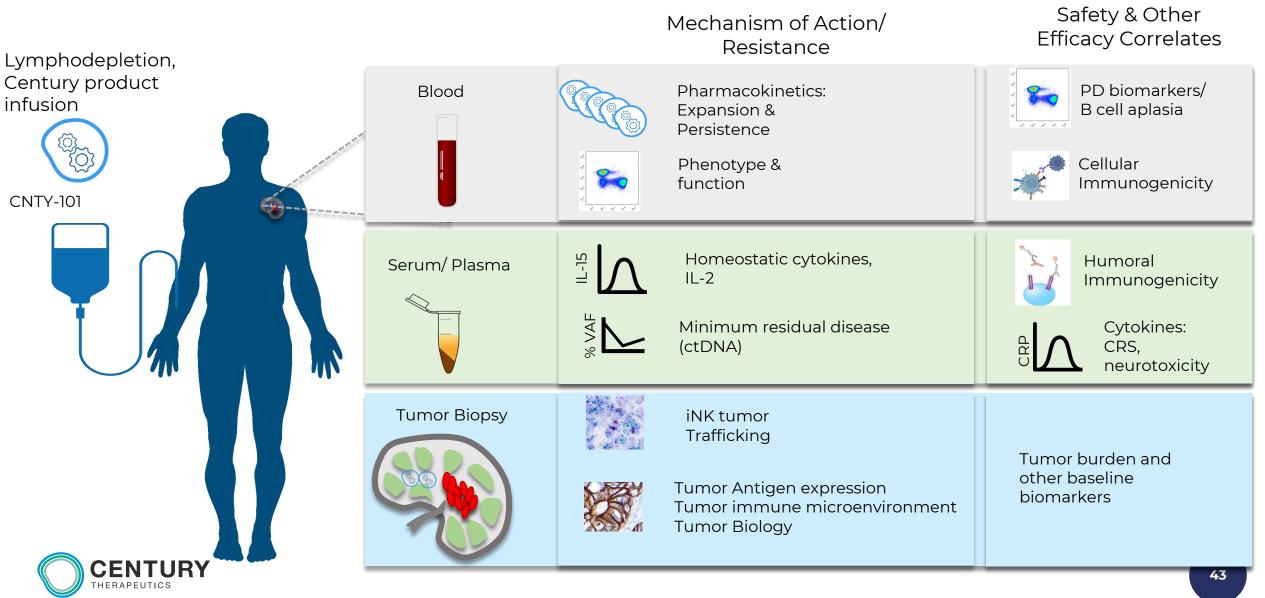


### TIMELINE (SINGLE DOSE) AND ASSESSMENTS

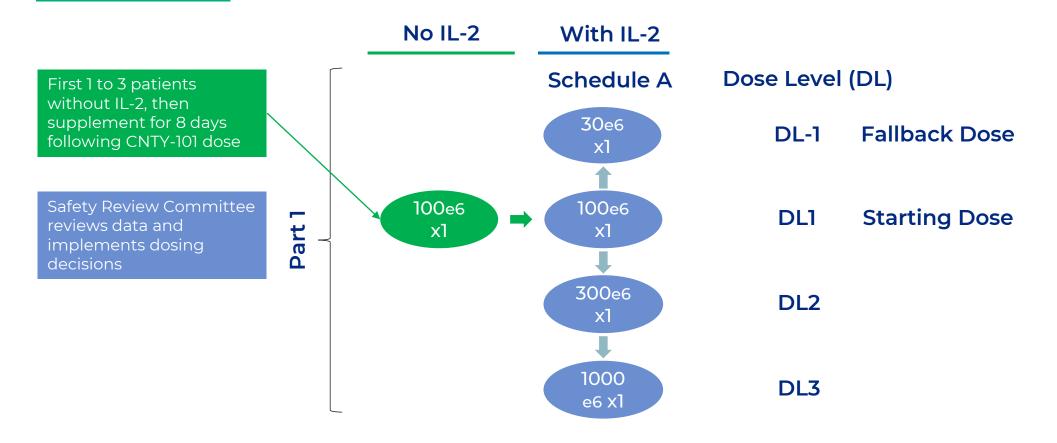




### **CNTY-101 EXPLORATORY STUDIES WITHIN ELIPSE-1**

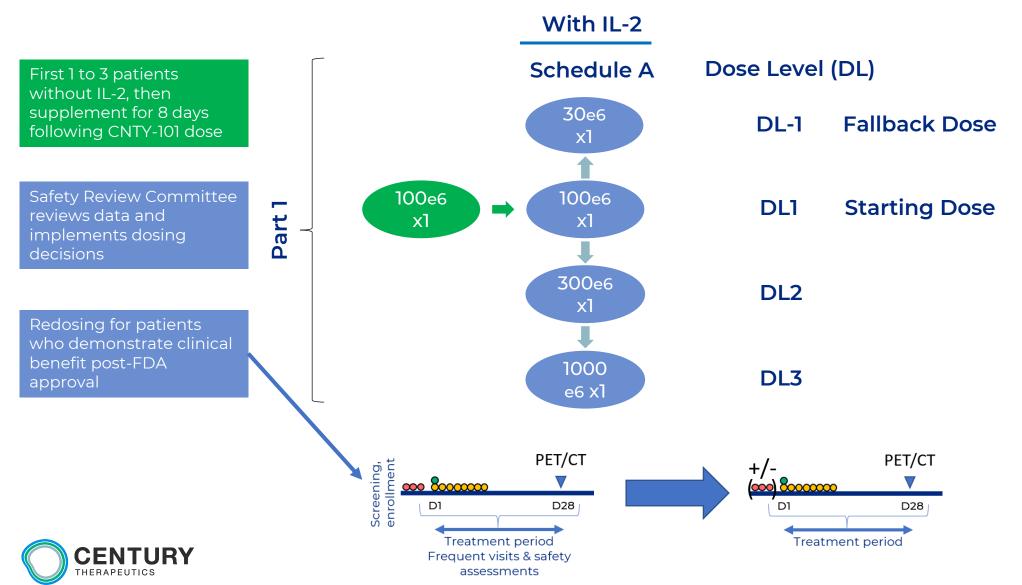


### ELIPSE-1 TREATMENT SCHEMA (1) EVALUATION OF SINGLE DOSE ESCALATION AND IL-2

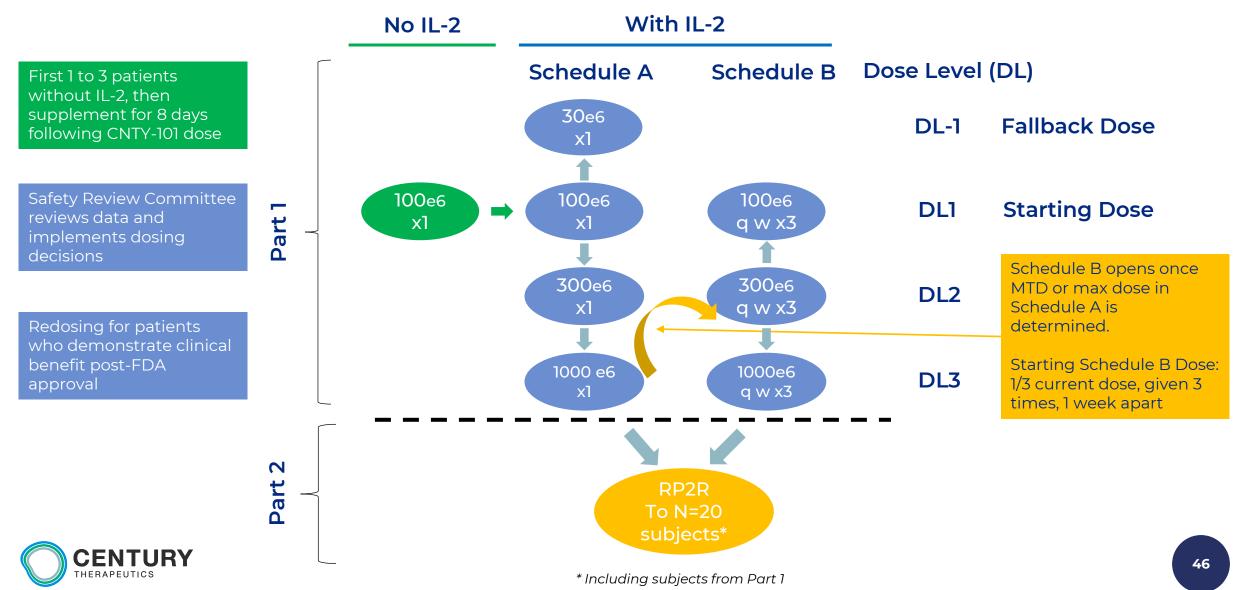




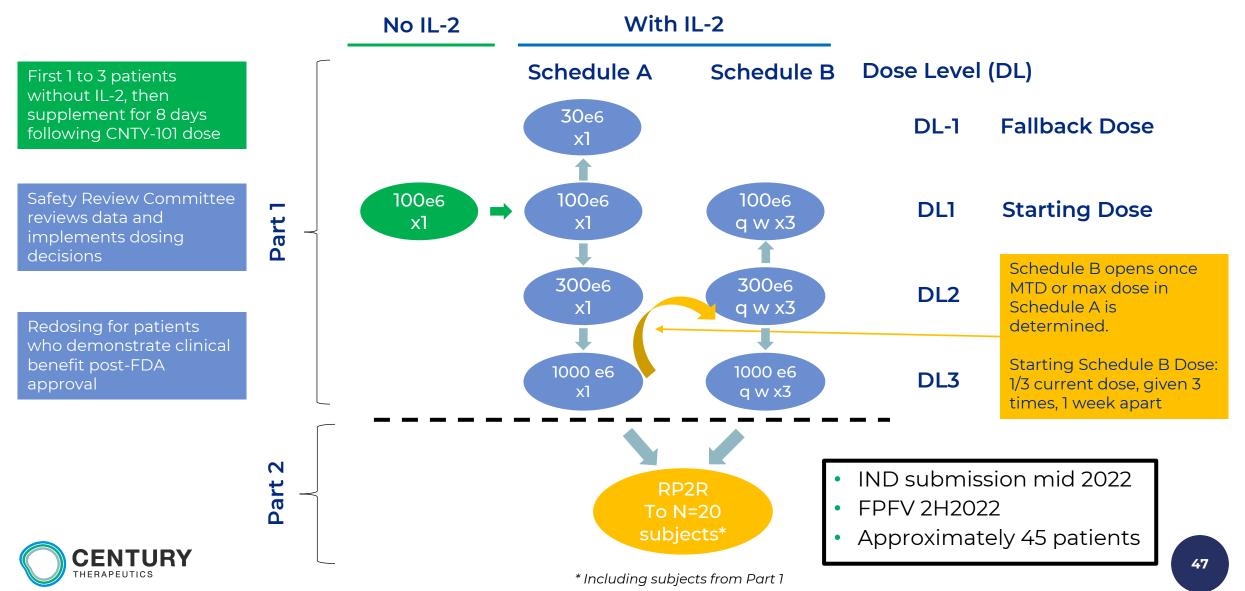
### ELIPSE-1 TREATMENT SCHEMA (2) EVALUATION OF ADDITIONAL CYCLE(S)



### ELIPSE-1 TREATMENT SCHEMA (3) EVALUATION OF MULTIPLE DOSING SCHEDULE



### ELIPSE-1 TREATMENT SCHEMA (4) KEY MILESTONES



### **SUMMARY**

#### Century's iPSC-derived NK cell therapies - CNTY-101

- Precise, multiple genome edits
- Unlimited supply
- Homogeneous product
- Off-the-shelf
- Allo-evasion ELiPSE-1
- Potential for excellent safety profile and outpatient treatment ELIPSE-1
- Potential for promising efficacy, access to redosing and re-treatment cycles ELIPSE-1

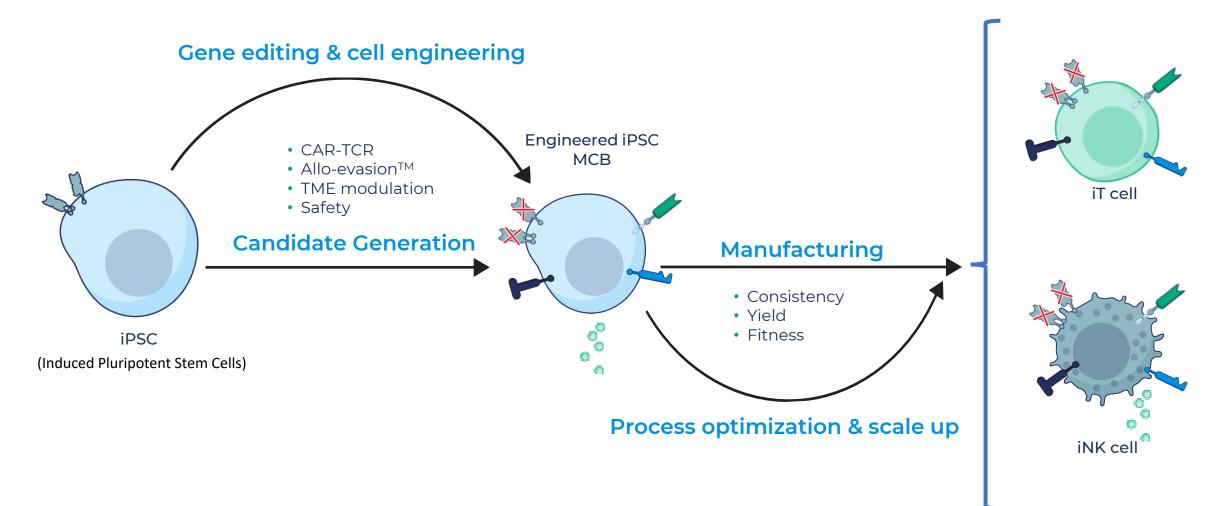


### **CENTURY IT PLATFORM UPDATE**

### Luis Borges, PhD | CSO



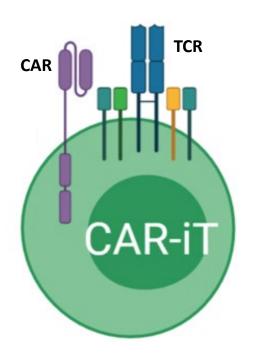
## AT CENTURY, WE ENGINEER iPSCs TO GENERATE IT AND INK CELL CANCER THERAPIES





### CENTURY'S IT CELL PLATFORM THE CONCEPT OF TrueT CELLS EXPRESSING TRUSTED TCRs

TrueT cells



#### T cells express two major types of TCRs

- **αβ TCRs:** recognize hypervariable peptide antigens in the context of MHC molecules; responsible for GvHD
- **γδ TCRs;** recognize invariant antigens such as phosphoantigens independently of MHC molecules; no GvHD

### **TrueT cells express Trusted TCRs**

- Trusted TCRs do not to induce GvHD
  - γδ TCR
  - Shared viral-specific  $\alpha\beta$  TCRs
- Trusted TCRs improve iPSC T cell differentiation and might improve in vivo persistence and functionality

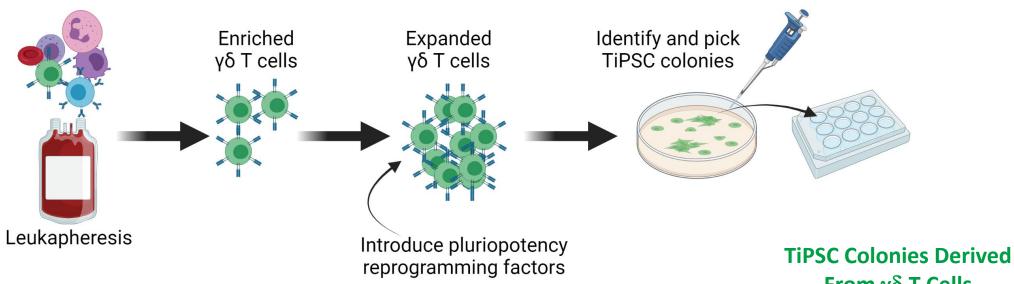


### $\gamma\delta$ T CELLS SHARED PROPERTIES OF ADAPTIVE AND INNATE IMMUNE CELLS AND OFFER UNIQUE ADVANTAGES FOR CANCER THERAPY

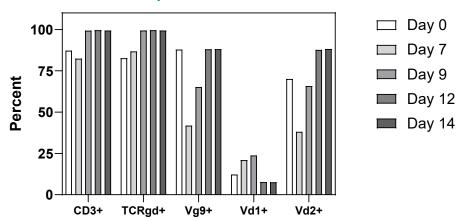
Property	lphaeta T cells	γδ T cells
Low risk of GvHD	-	$\checkmark$
Innate anti-tumor killing	-	$\checkmark$
TCR-mediated tumor killing	$\checkmark$	$\checkmark$
MHC-independence for TCR- mediated killing	-	$\checkmark$
Recognition of molecular patterns of tumor cell distress	-	$\checkmark$
Low risk of CRS	-	$\checkmark$



## CENTURY HAS GENERATED MULTIPLE TIPSC LINES THROUGH THE REPROGRAMING OF $\gamma\delta$ T CELLS



#### **Expansion Of** $\gamma\delta$ **T Cells From Blood**

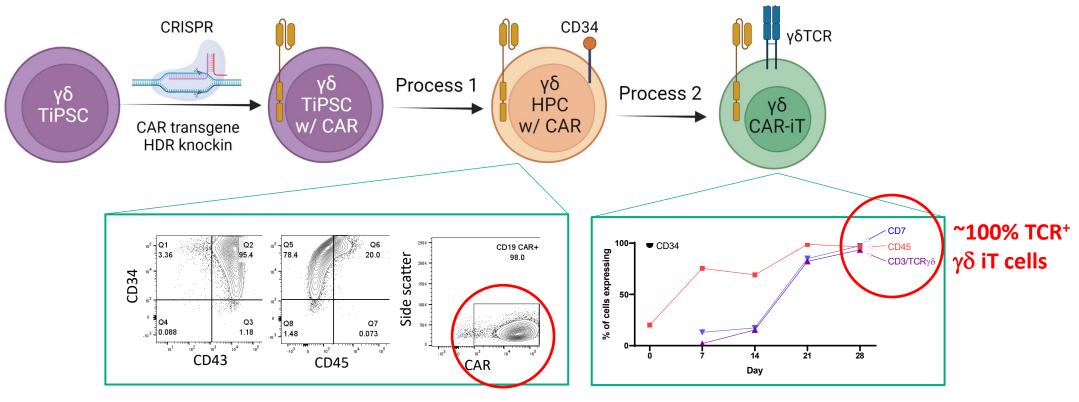




### From $\gamma\delta$ T Cells



## CENTURY HAS DEVELOPED HIGHLY REPRODUCIBLE PROTOCOLS TO DIFFERENTIATE $\gamma\delta$ TiPSC LINES

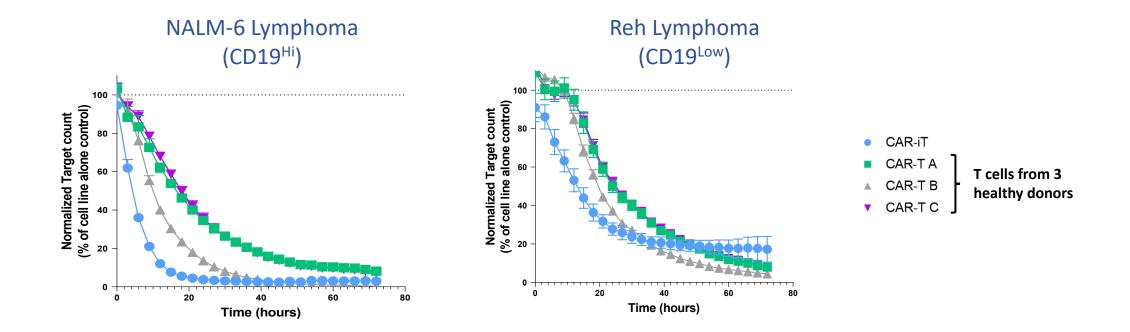


98% CAR<sup>+</sup> cells



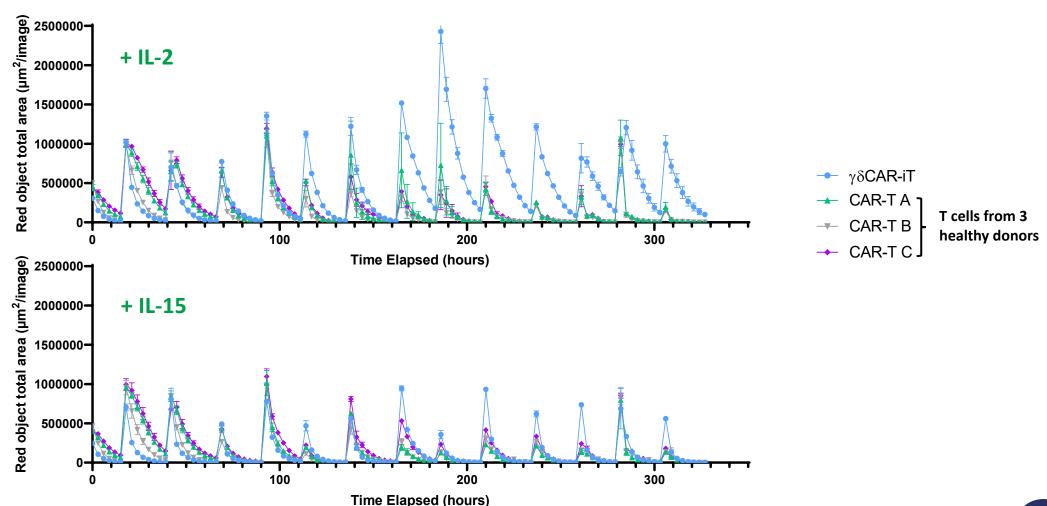
## $\gamma\delta$ CAR-iT CELLS KILL TUMORS AS EFFICIENTLY OR BETTER THAN CAR-T CELLS

#### γδ CAR-iT Cells Kill Multiple Lymphoma Cell lines Expressing Different Levels Of CD19





### $\gamma\delta$ CAR-it cells kill lymphoma cells through multiple rounds of killing without reaching exhaustion

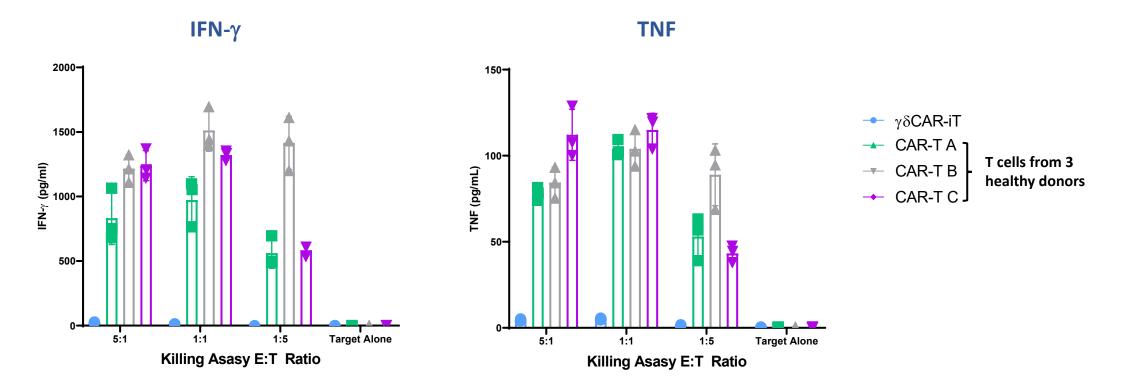


Serial Killing CD19<sup>+</sup> Lymphoma Cells



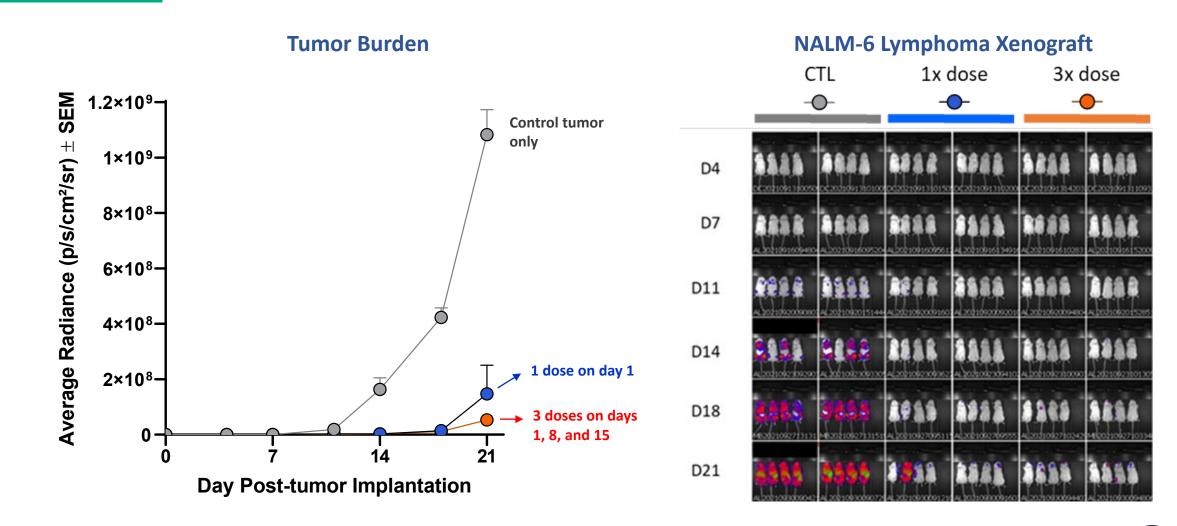
### $\gamma\delta$ CAR-iT CELLS DO NOT RELEASE INFLAMMATORY CYTOKINES WHEN KILLING TARGETS

Unlike Conventional CAR-T Cells, γδ CAR-iT Cells Did Not Release IFN-γ Or TNF When Interacting With Tumors Cells





## CENTURY'S CAR- $\gamma\delta$ it cells have robust anti-lymphoma activity in vivo

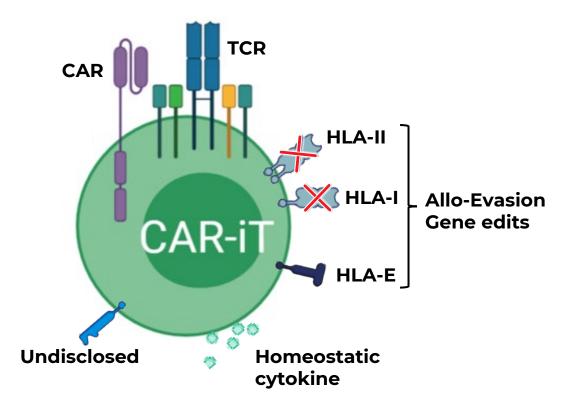




### **NEXT STEPS**

- Complete the reprograming of clinical grade  $\gamma \delta$ TiPSC lines from multiple donors
- Engineer core features on novel  $\gamma\delta$  T-IPSC lines to generate a common TiPSC progenitor for multiple iT cell product candidates
- Generate new iT product candidates for solid tumors and heme malignancies

### $\gamma\delta$ iT Product Candidates Will Include Multiple Gene Edits





### CENTURY'S iPSC-DERIVED $\gamma\delta$ T CELLS IN ACTION



# THANK YOU





