



# Immune-Evasive Universal CAR T-cell

**ASGCT 2022**

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**Vice President Gene Therapy**

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# FORWARD-LOOKING STATEMENTS

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This presentation contains “forward-looking” statements within the meaning of applicable securities laws, including the Private Securities Litigation Reform Act of 1995. Forward-looking statements may be identified by words such as “at this time,” “anticipate,” “believe,” “expect,” “on track,” “plan,” “scheduled,” and “will,” or the negative of these and similar expressions.

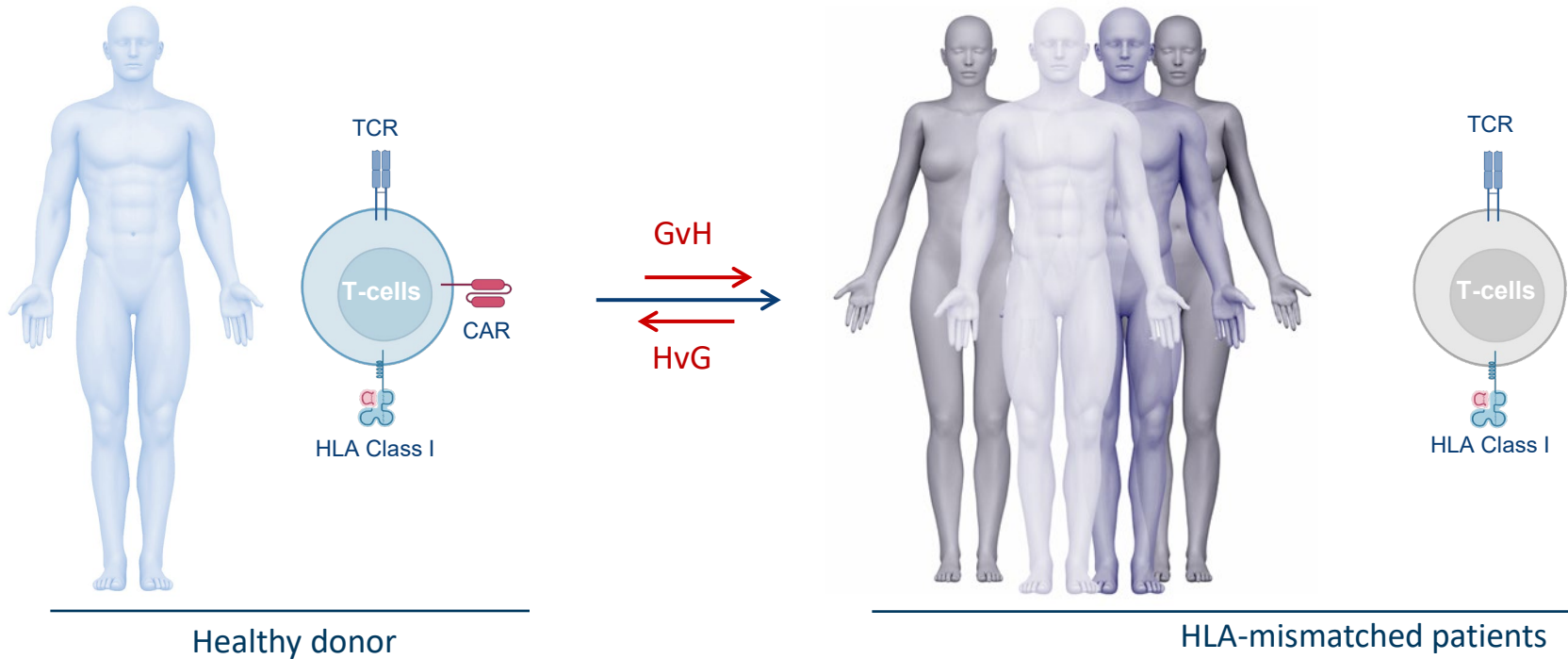
These forward-looking statements, which are based on our management’s current expectations and assumptions and on information currently available to management, include statements about our research and development projects and priorities, our pre-clinical project development efforts, the timing and progress of clinical trials (including with respect to patient enrollment and follow-up), the timing of our presentation of data, the adequacy of our supply of clinical vials, the timing of completion of construction of our Raleigh, North Carolina manufacturing facility, and operational capabilities at our manufacturing facilities, and the sufficiency of cash to fund operations.

These forward-looking statements are made in light of information currently available to us and are subject to numerous risks and uncertainties, including with respect to the numerous risks associated with biopharmaceutical product candidate development as well as the duration and severity of the COVID-19 pandemic and governmental and regulatory measures implemented in response to the evolving situation.

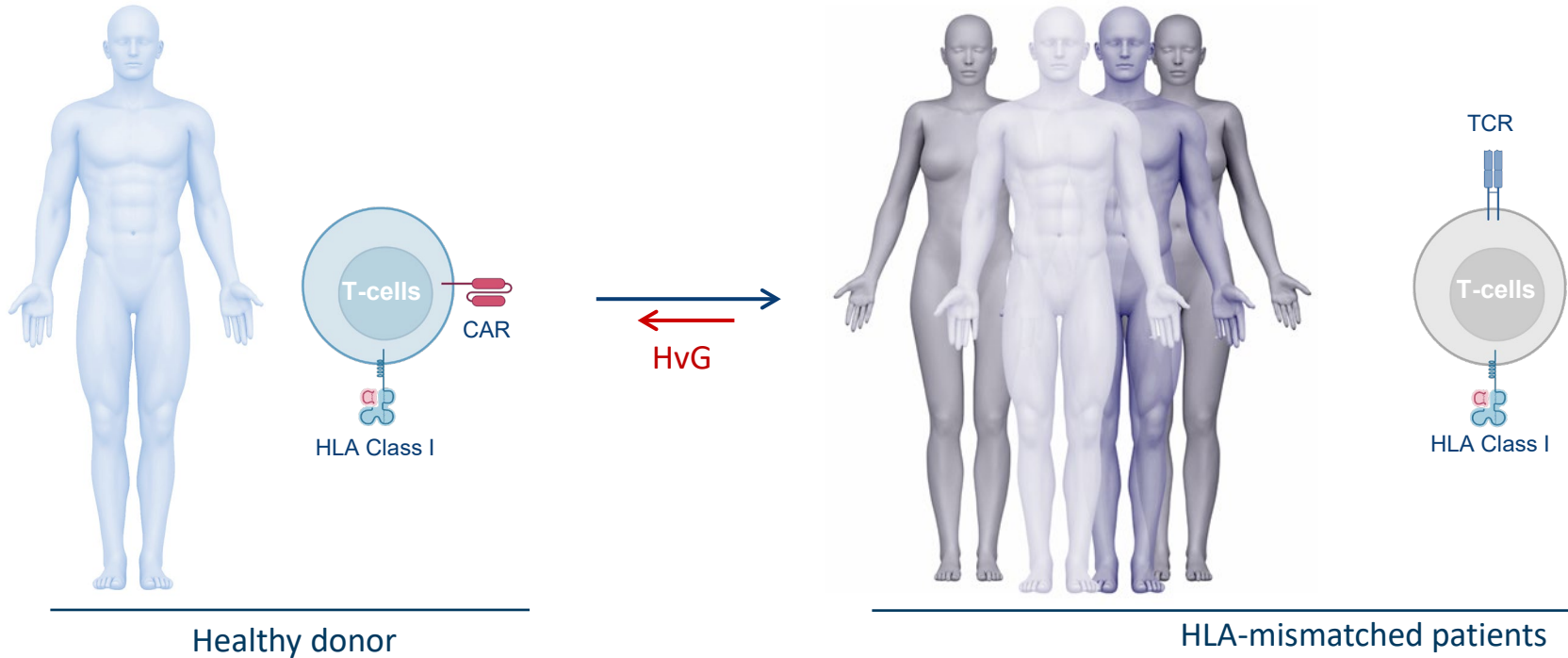
With respect to our cash runway, our operating plans, including product development plans, may change as a result of various factors, including factors currently unknown to us. Furthermore, many other important factors, including those described in our Annual Report on Form 20-F and the financial report (including the management report) for the year ended December 31, 2021 and subsequent filings Collectis makes with the Securities Exchange Commission from time to time, as well as other known and unknown risks and uncertainties may adversely affect such forward-looking statements and cause our actual results, performance or achievements to be materially different from those expressed or implied by the forward-looking statements. Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons why actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future.

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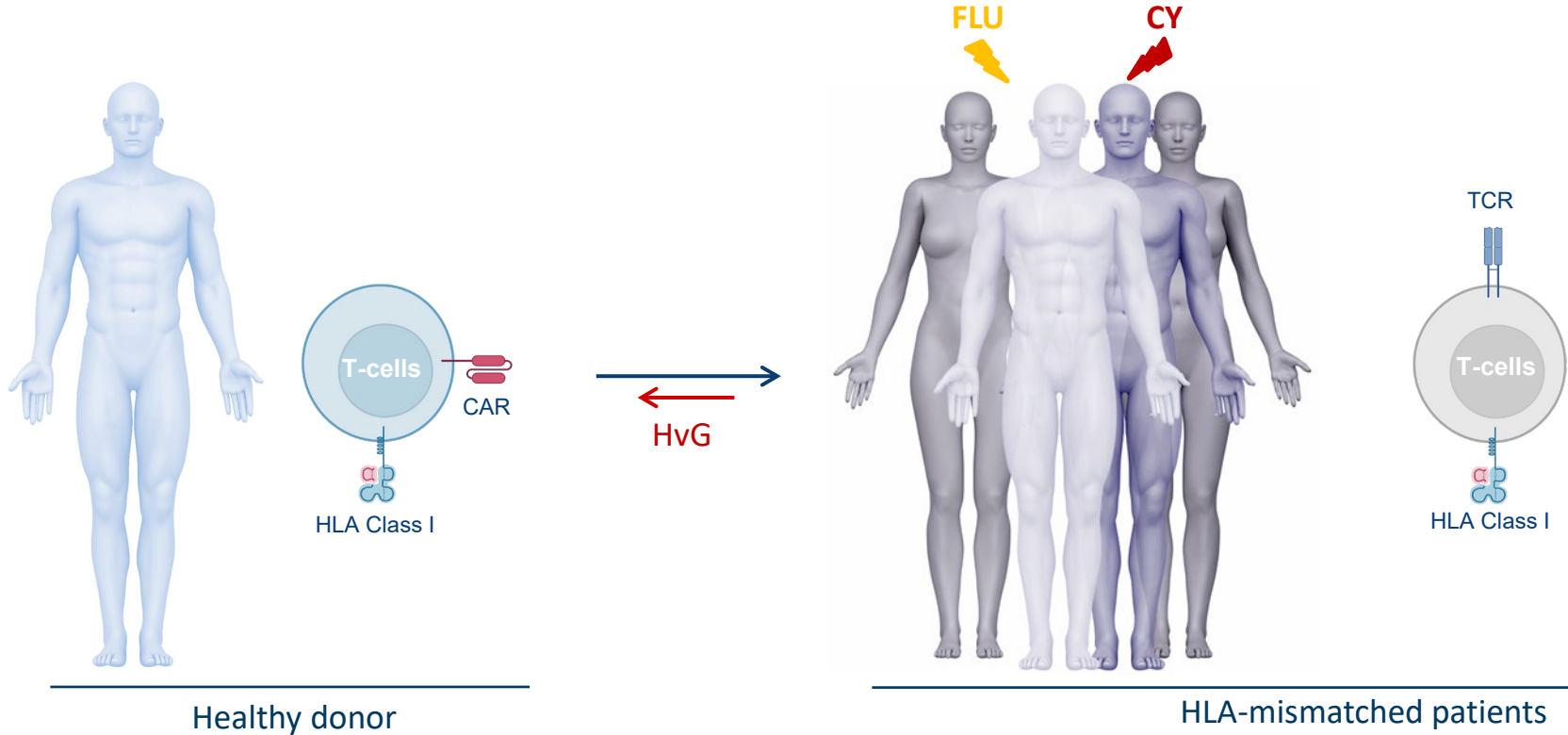
# UCART Cell Adoptive Transfer in Allogeneic Settings



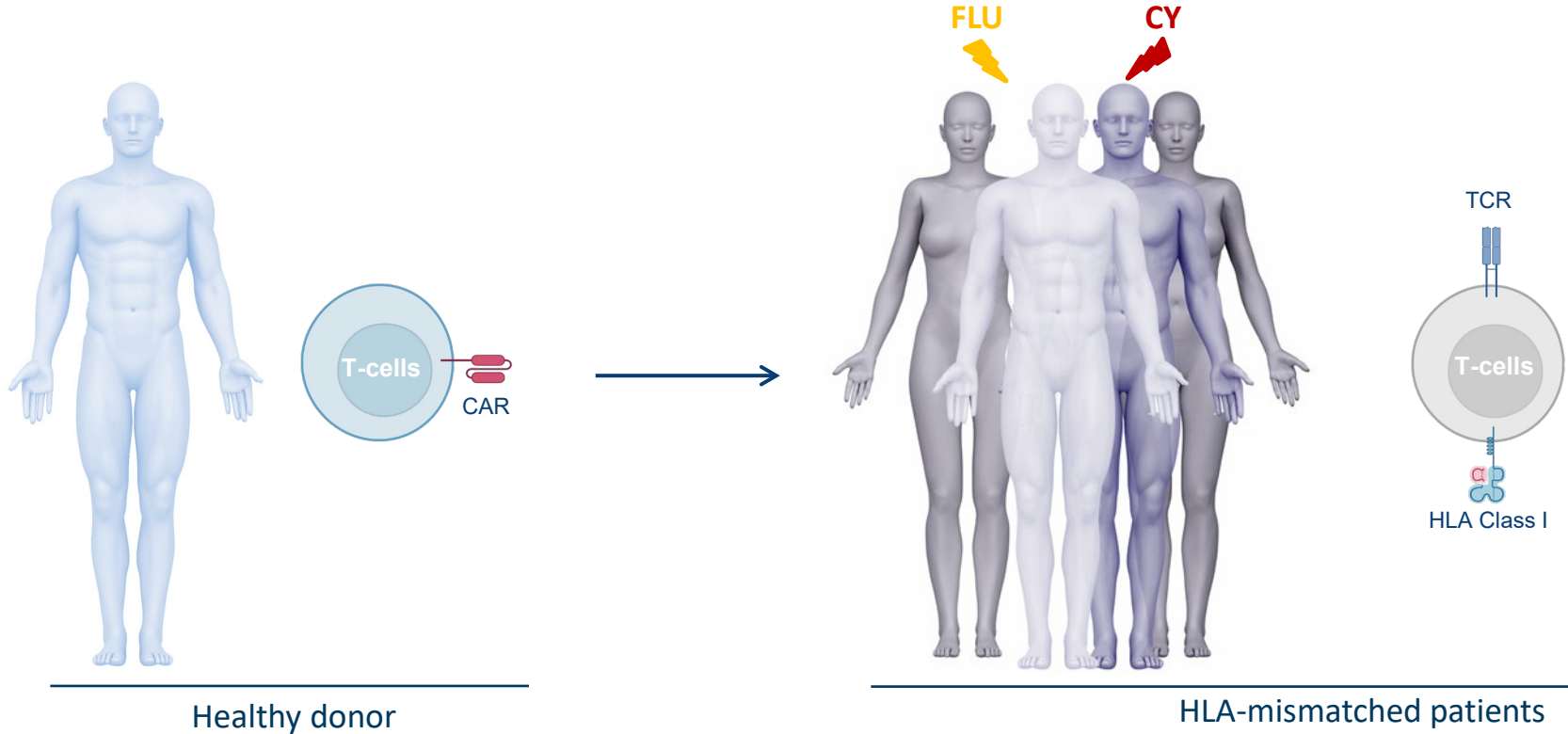
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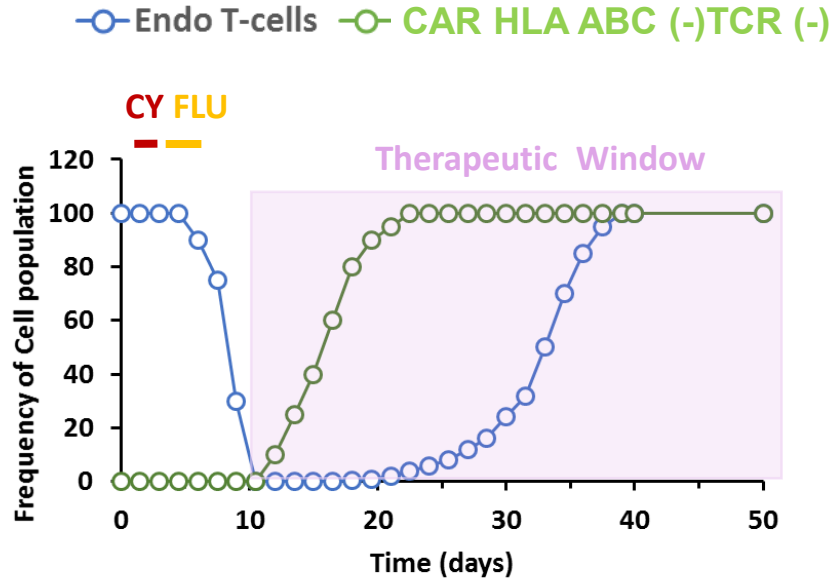
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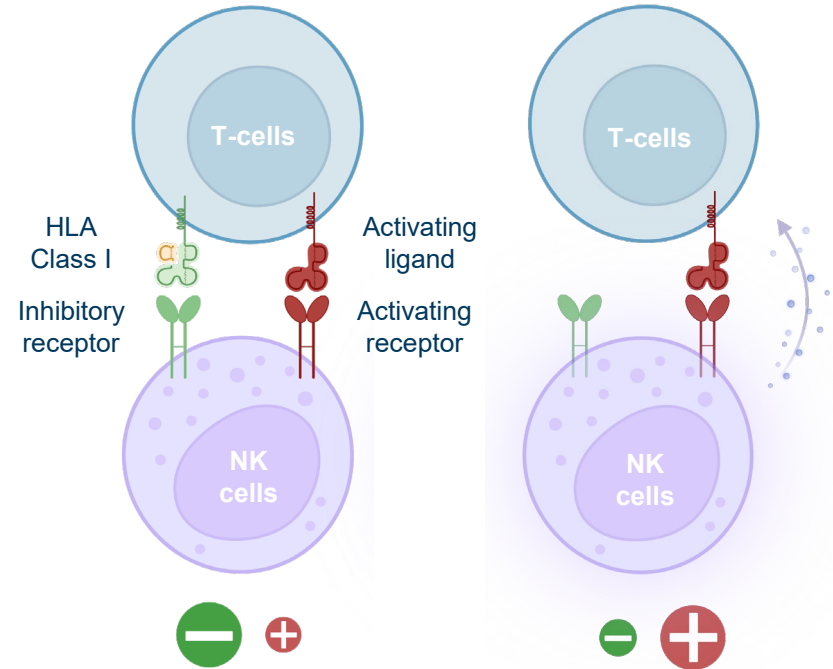


# UCART Cell Adoptive Transfer in Allogeneic Settings



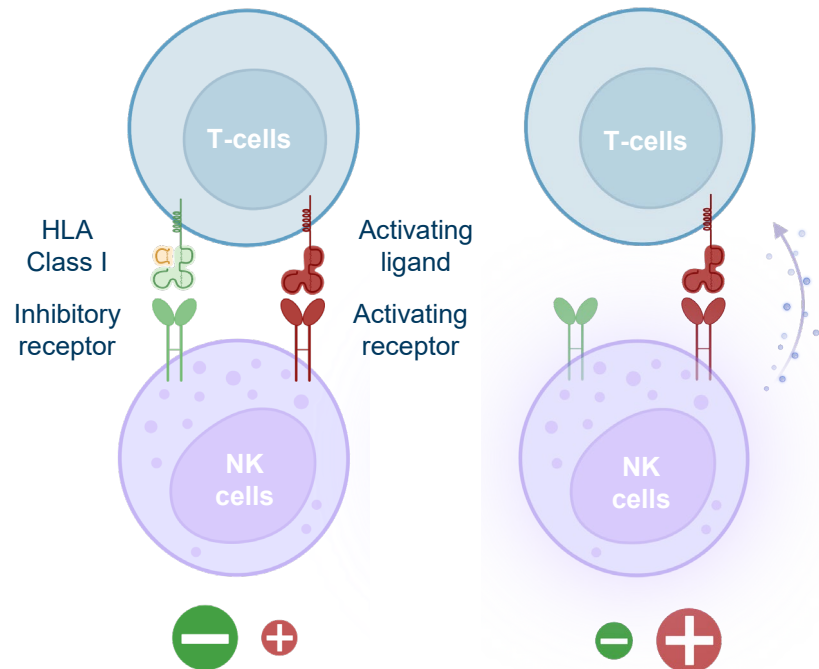
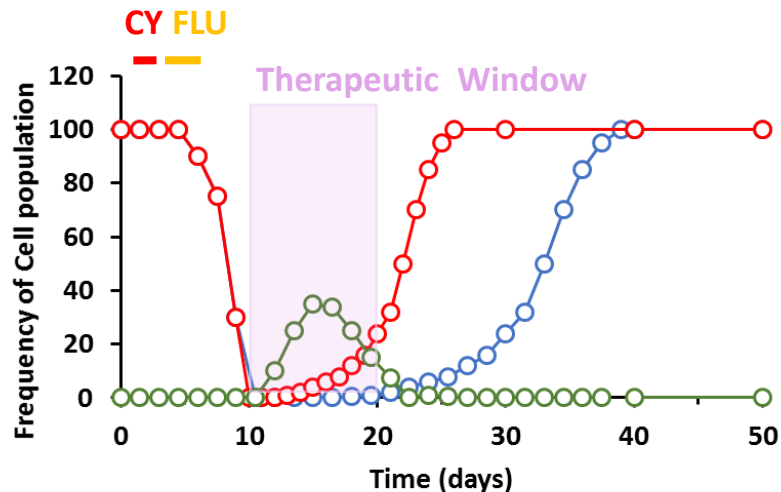
## Pros

- Prevents endogenous T-cell attack
- Does not rely on long term lymphodepletion
- Spares cancer-specific host immune cells



# UCART Cell Adoptive Transfer in Allogeneic Settings

○ Endo T-cells    ○ Endo NK cells    ○ CAR HLA-ABC (-)TCR (-)



## Pros

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- -Does not rely on long term lymphodepletion
- -Sparses cancer-specific host immune cells

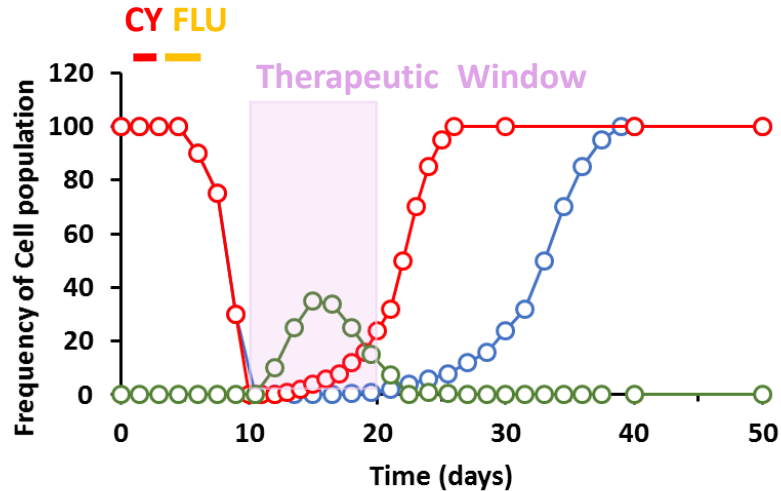
## Cons

- NK missing self

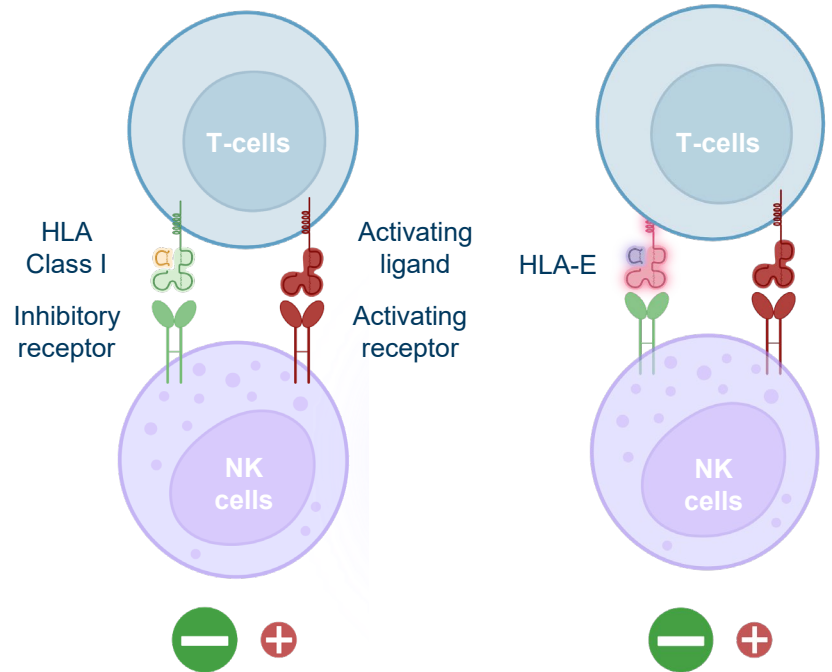


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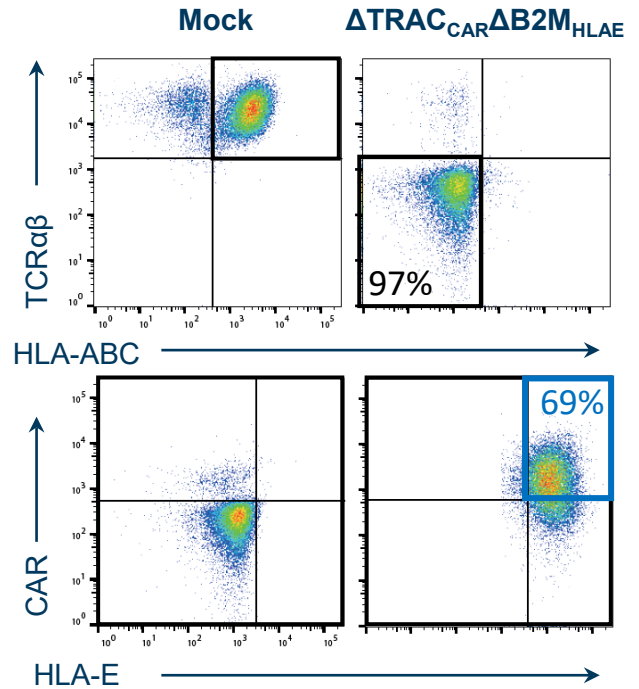
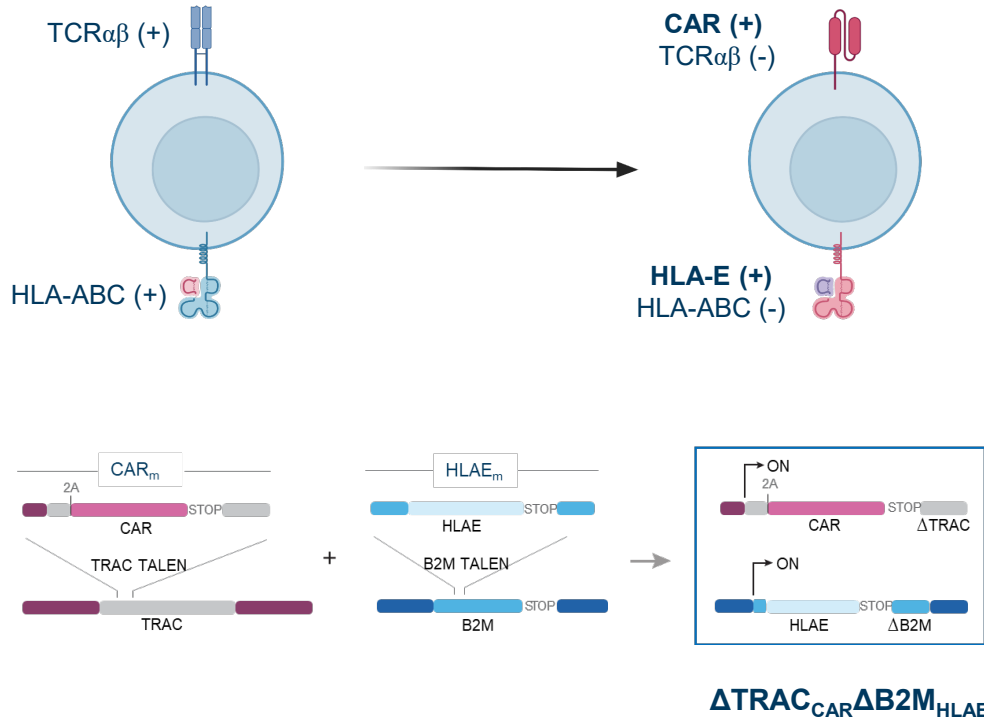
○ Endo T-cells   
 ○ Endo NK cells   
 ○ CAR HLA-ABC (-) TCR (-) HLA-E (+)



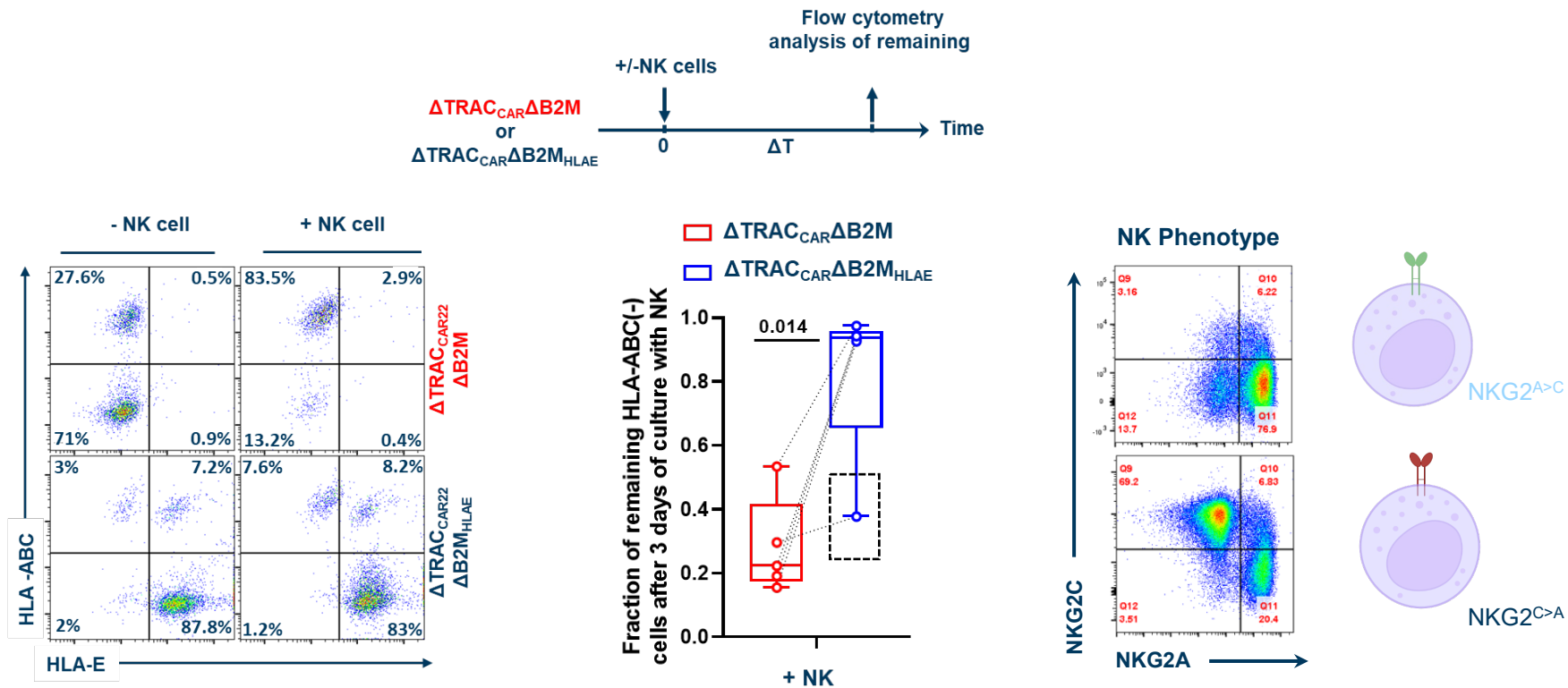
**Potential solution to missing self reaction**  
 -Expression of the non-polymorphic HLA molecule HLA-E



# TALEN®-Mediated Engineering of Immune-Evasive UCART Cells

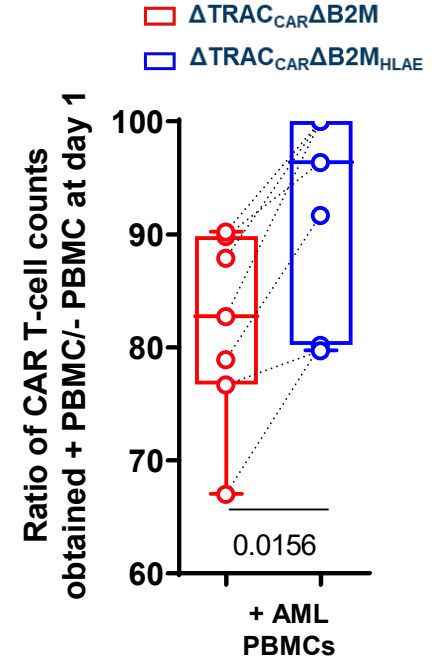
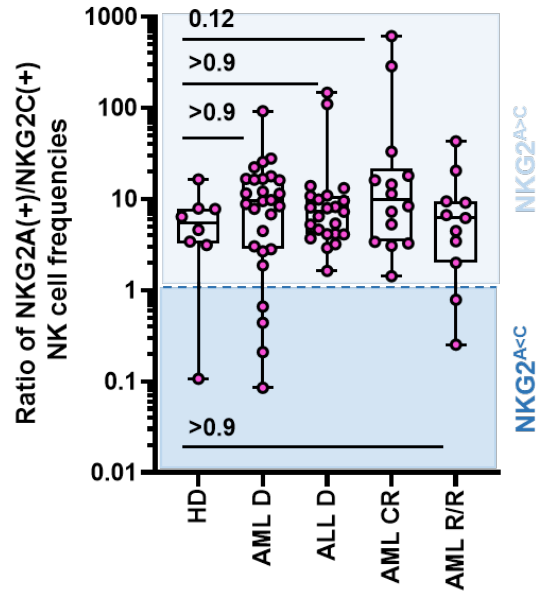
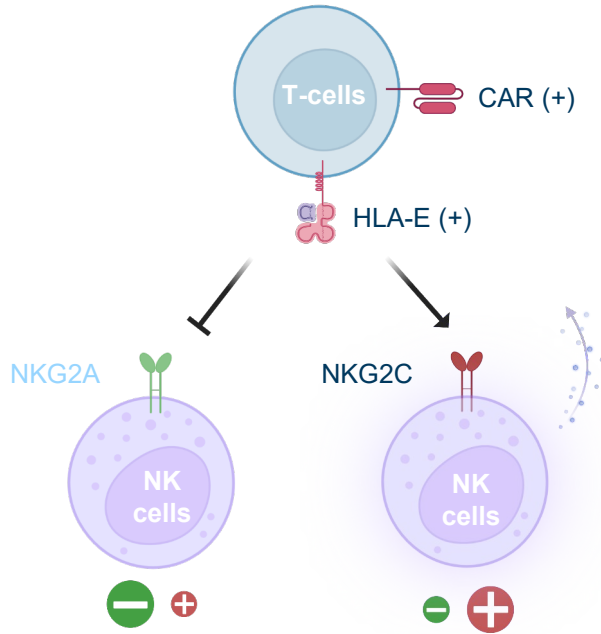


# Immune-Evasive UCART Cell Resists to Healthy Donor NK Cells



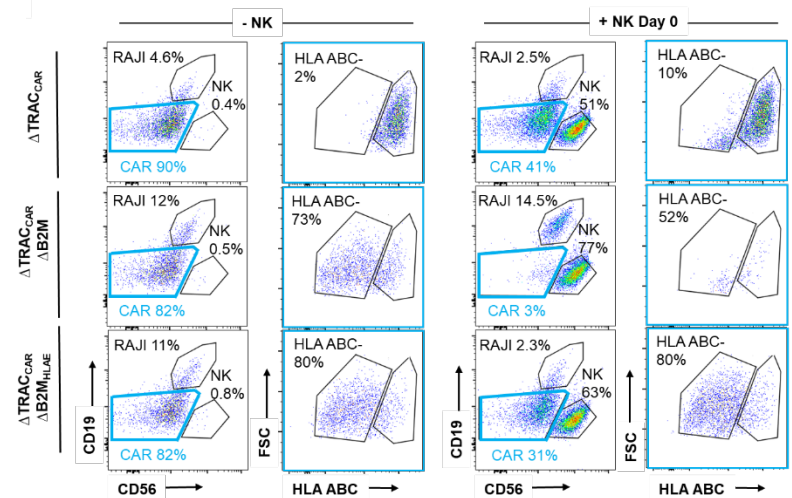
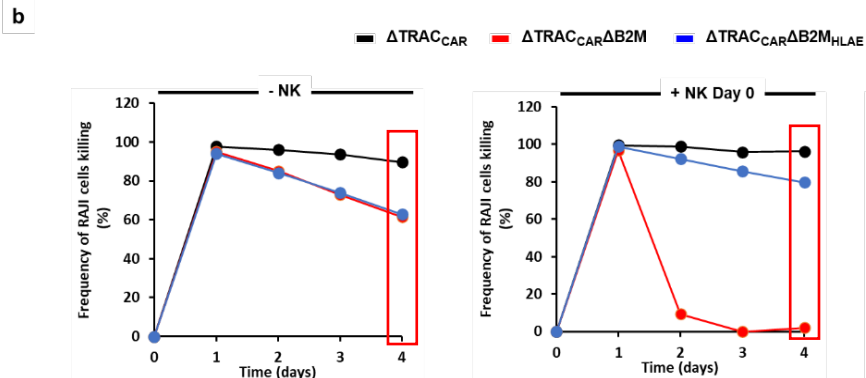
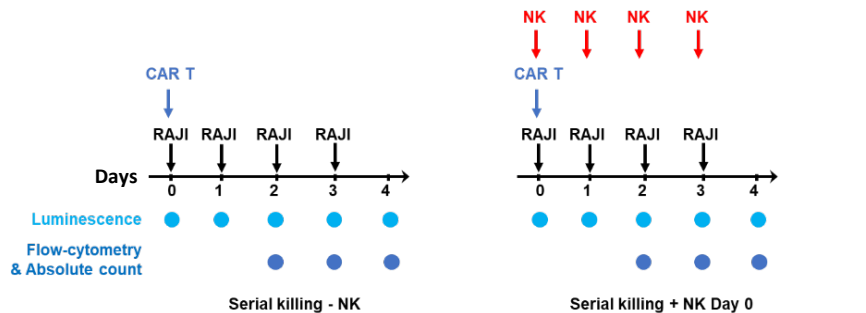
$\Delta\text{TRAC}_{\text{CAR}}\Delta\text{B2M}_{\text{HLAE}}$  cells resist to NK cells from the vast majority of healthy donors

# The Immune-Evasive Properties of UCART Depend on the NKG2A/C Ratio



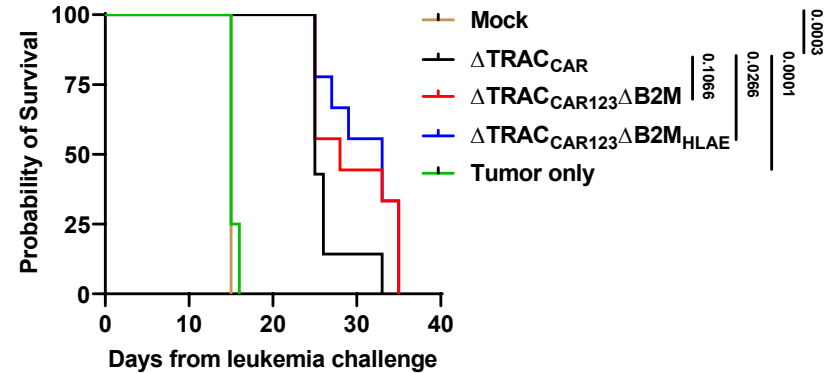
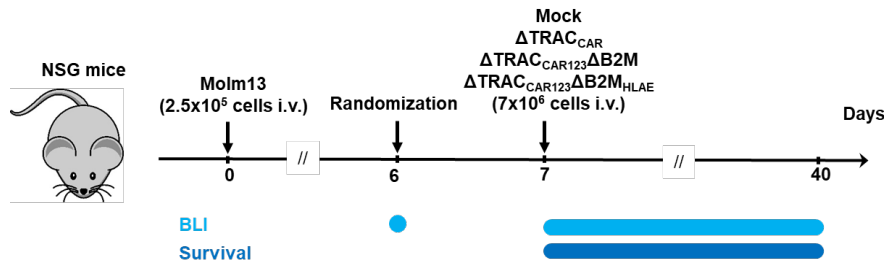
$\Delta\text{TRAC}_{\text{CAR}}\Delta\text{B2M}_{\text{HLAE}}$  is likely to resist to NK cells from the vast majority of HD/AML/ALL patients

# Immune-Evasive UCART Shows Antitumor Activity In The Presence Of NK Cells



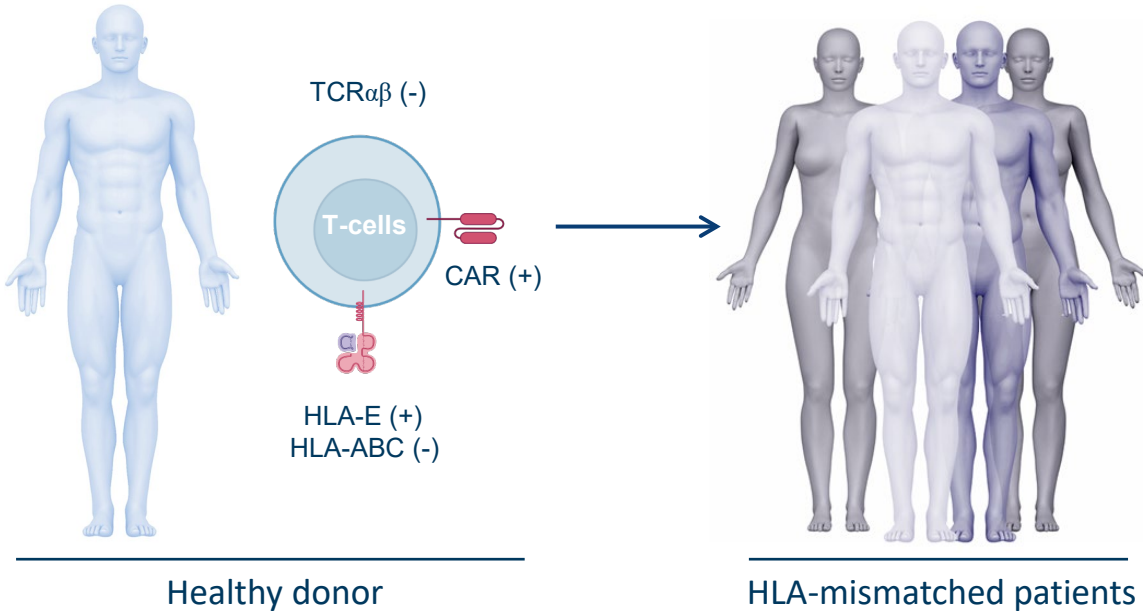
HLAE prolongs antitumor activity of  $\Delta TRAC_{CAR\Delta B2M}$  cells in the presence of NK cells

# Immune-Evasive UCART Cell Shows Antitumor Activity in vivo



Multiplex editing does not affect ΔTRAC<sub>CAR</sub>ΔB2M<sub>HLAE</sub> antitumor activity in vivo

# Conclusions



## Immune-evasive Universal CAR T-cells

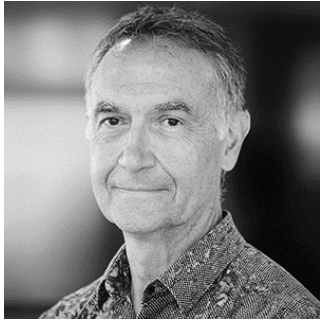
Prevent attack of host tissue (GvHD)

Prevent depletion (HvG)

- by host NK cells (NKG2<sup>A>C</sup>)
- by alloreactive host T-cell

Show antitumor activity on par with  $\Delta$ TRAC<sub>CAR</sub> cells

# Acknowledgments



Daniel Olive



Anne-Sophie  
Chretien



Aude Le Roy



Raynier Devillier



Emanuela Marcenaro

Thomas  
Pagliardini



and most importantly, we thank the patients





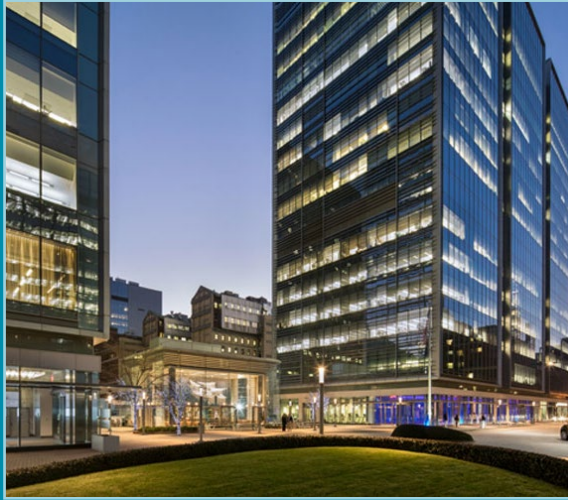
# THANK YOU

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