



# CB-010 Clinical Program Update

May 12, 2022



Transformative genome-edited therapies for patients

# Forward-looking statements

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As a result of many factors, including risks related to our limited operating history, history of net operating losses, financial position and our ability to raise additional capital as needed to fund our operations and product candidate development; uncertainties related to the initiation, cost, timing, and progress, and results of our current and future research and development programs, preclinical studies, and clinical trials; risks that initial or interim clinical trial data will not ultimately be predictive of the safety and efficacy of our product candidates or that clinical outcomes may differ as more clinical data becomes available; our ability to obtain and maintain regulatory approval for our product candidates; risks that our product candidates, if approved, may not gain market acceptance due to negative public opinion and increased regulatory scrutiny of cell therapies involving genome editing; our ability to meet future regulatory standards with respect to our products; our ability to establish and/or maintain intellectual property rights covering our product candidates and genome-editing technology; risks of third parties asserting that our product candidates infringe their patents; developments related to our competitors and our industry; our reliance on third parties to conduct our clinical trials and manufacture our product candidates; the impact of COVID-19 and geopolitical events on our business and operations; and other risks described in greater detail in our filings with the Securities and Exchange Commission (the "SEC"), including the section titled "Risk Factors" of our Annual Report on Form 10-K for the year ended December 31, 2021, and other filings we make with the SEC; the events and circumstances reflected in our forward-looking statements may not be achieved or may not occur, and actual results could differ materially from those described in or implied by the forward-looking statements contained in this presentation.

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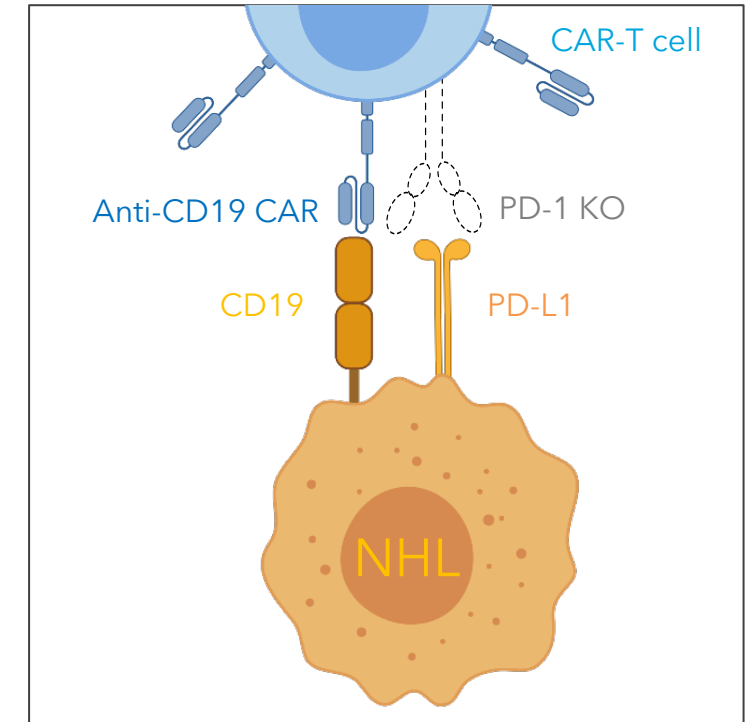
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# CB-010: anti-CD19 allogeneic CAR-T cell therapy

## Key attributes

	CB-010	Conventional allo anti-CD19 CAR-Ts
PD-1 KO for enhanced persistence of antitumor activity	✓	X
<ul style="list-style-type: none"> <li>Potentially better initial tumor debulking preclinically</li> <li>Potentially better therapeutic index</li> </ul>	✓	X
Site-specific insertion of CAR into <i>TRAC</i> locus	✓	Varies
<ul style="list-style-type: none"> <li>Eliminates random integration and reduces risk of GvHD</li> </ul>	✓	Varies
Cas9 chrDNA editing for enhanced genomic integrity	✓	X
<ul style="list-style-type: none"> <li>Reduced off-target editing and genomic rearrangements</li> </ul>	✓	X



## Program: CB-010

Tumor antigen: CD19

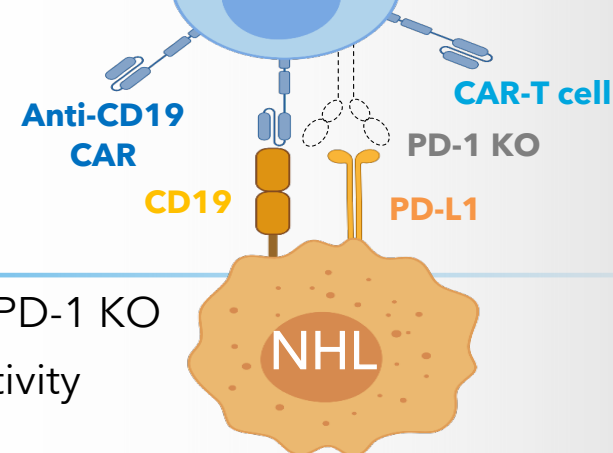
Healthy donor leukapheresis-derived T cells

Indication: r/r non-Hodgkin lymphoma (NHL)

Status: Phase 1

# Revolutionizing allogeneic cell therapies with CB-010: setting a new therapeutic bar

- Caribou believes CB-010 is the **1<sup>st</sup> allogeneic CAR-T cell therapy** in the clinic with a PD-1 KO
- PD-1 KO genome-editing strategy designed to **improve persistence** of antitumor activity



## CB-010: 1<sup>st</sup> allogeneic CAR-T cell therapy to achieve 100% ORR

Single dose at dose level 1\* (N=6)

**AT 28 DAYS**

5 patients evaluable for efficacy<sup>1</sup>



**100% ORR**

5/5 patients



**80% CR**

4/5 patients



**r/r B-NHL patients in ANTLER** had aggressive disease (median 3 prior treatments)

**Generally well tolerated** with AEs as expected for autologous/allogeneic anti-CD19 CAR-T cell therapies

**Longer duration data** from dose level 1 (N=6) slated for EHA; **additional ANTLER data** expected by YE 2022

**Enrolling patients** at dose level 2<sup>†</sup> → planning for future development

\* 40x10<sup>6</sup> CAR-T cells ; † 80x10<sup>6</sup> CAR-T cells

<sup>1</sup> All data as of Feb 23, 2022 data cutoff date, data collection ongoing, efficacy measured by Lugano criteria

Source: Abstract for European Hematology Association (EHA) 2022 Hybrid Congress

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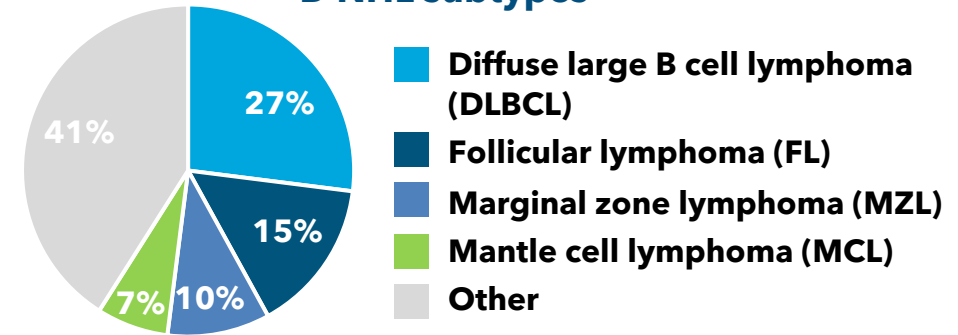
A 3D scientific illustration of a cell. The cell is spherical and covered in various receptors and proteins on its surface. Inside the cell, there are numerous small yellow and blue molecules, some of which appear to be interacting with the internal structures. The background is a dark blue gradient with faint, larger-scale cell-like structures.

**LEAD PROGRAM CB-010**  
ANTLER Phase 1 trial

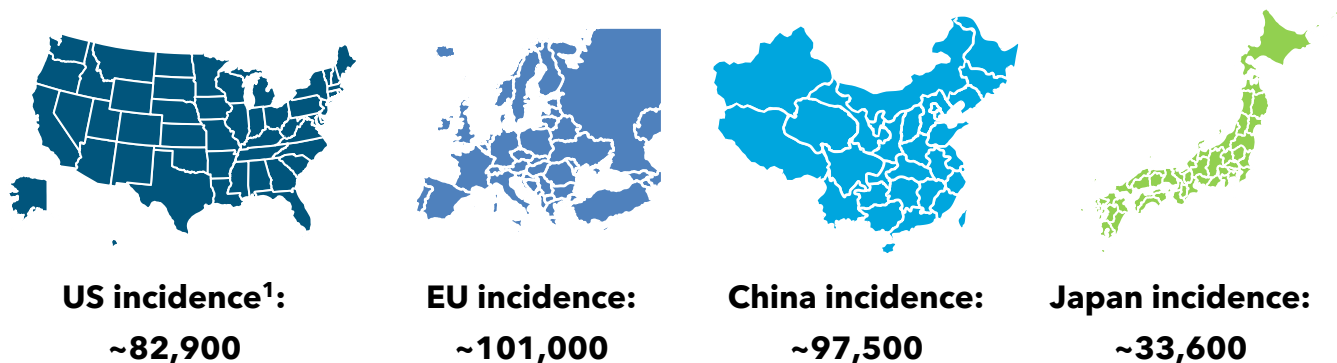
# r/r B-NHL: high unmet need globally for off-the-shelf cell therapy

- NHL is the most common hematologic malignancy in the U.S.
- Mature B cell lymphomas (B-NHL) are 80-85% of all NHL cases
- ~34% of B-NHL cases are considered relapsed or refractory (r/r)<sup>1</sup>
- Current autologous CAR-T cell therapies have limited patient access with complex manufacturing and high production costs

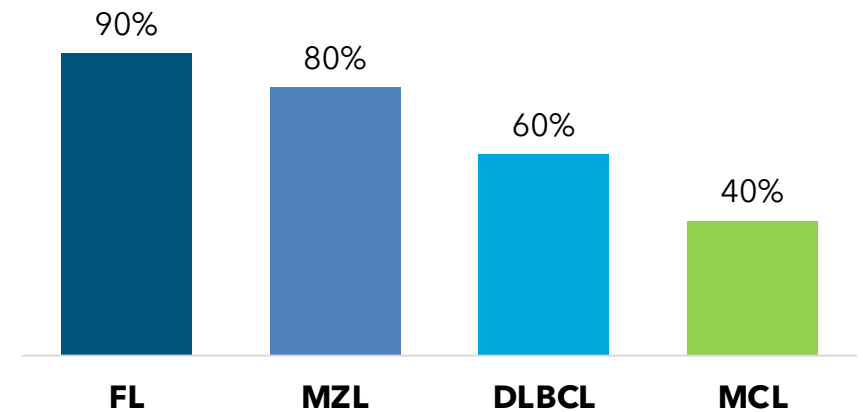
**B-NHL subtypes<sup>1</sup>**



**Worldwide NHL incidence<sup>2</sup>**



**B-NHL 5-year post-diagnosis survival rates<sup>3</sup>**



<sup>1</sup> National Cancer Institute, Leukemia & Lymphoma Society, Lymphoma Research Foundation

<sup>2</sup> Evaluate Pharma, May 2022, [www.evaluate.com](http://www.evaluate.com)

<sup>3</sup> Cancer Research U.K.

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# CB-010 ANTLER Phase 1 trial design

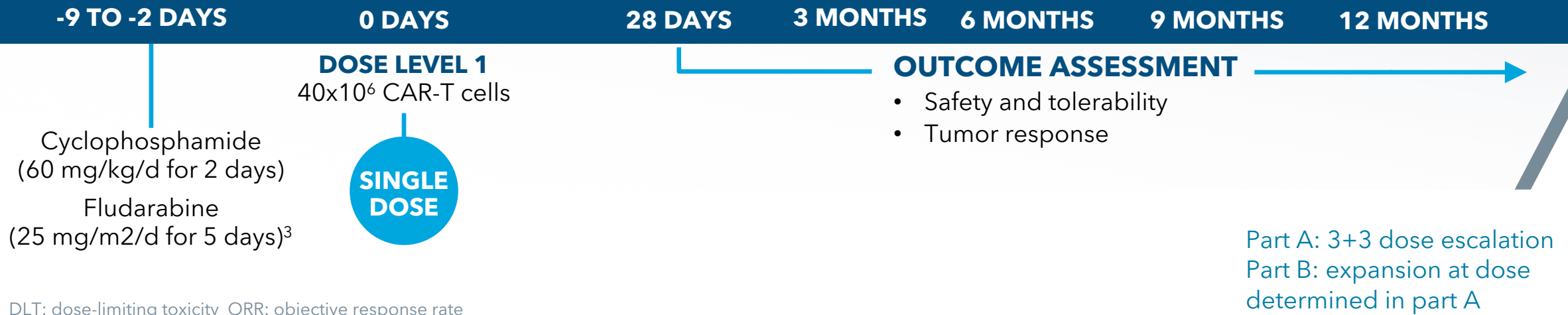
## Patients with aggressive disease

- **r/r B-NHL** (DLBCL, HGBL, tFL, PMBCL, FL<sup>1</sup>, MZL<sup>2</sup>, MCL)
- ≥2 prior lines of chemoimmunotherapy
- Exclusion: prior CD19-targeted therapy

## r/r B-NHL

### LYMPHODEPLETION

### CB-010



DLT: dose-limiting toxicity ORR: objective response rate

<sup>1</sup> Aggressively behaving, with POD24 (high risk)

<sup>2</sup> High grade

<sup>3</sup> Clin Cancer Res. 2011 July 1; 17(13): 4550-4557. doi:[10.1158/1078-0432.CCR-11-0116](https://doi.org/10.1158/1078-0432.CCR-11-0116).

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# ANTLER enrolled difficult-to-treat r/r B-NHL patients

Patient characteristics	Cohort 1 Dose level 1 (40x10 <sup>6</sup> CAR-T cells) (N=6)
Non-Hodgkin lymphoma subtype:	
DLBCL	2
FL <sup>1</sup>	2
MCL	1
PMBCL	1
Prior treatments	
Median number (range)	3 (2-8)

**ANTLER only enrolled patients with aggressive disease**

<sup>1</sup> Aggressively behaving, with POD24 (high risk)

Source: Abstract for European Hematology Association (EHA) 2022 Hybrid Congress

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# CB-010 generally well tolerated at dose level 1

- No cases of graft versus host disease (GvHD)
- Most AEs were Grade 1 or Grade 2
- No  $\geq$ Grade 2 CRS
- Single case of Grade 3 ICANS
  - Case characterized as dose-limiting toxicity
  - Patient received tocilizumab and steroids and recovered within 39 hours

28-day period AEs (Grade 3 or 4)	Cohort 1 <sup>1</sup> Dose level 1 (40x10 <sup>6</sup> CAR-T cells) (N=6)
Neutropenia	3 (50%)
Thrombocytopenia	2 (33%)
Anemia	1 (17%)
Hypogammaglobulinemia	1 (17%)
ICANS	1 (17%)

**Adverse events as expected for autologous or allogeneic anti-CD19 CAR-T cell therapies**

CRS: cytokine release syndrome ICANS: immune effector cell-associated neurotoxicity syndrome

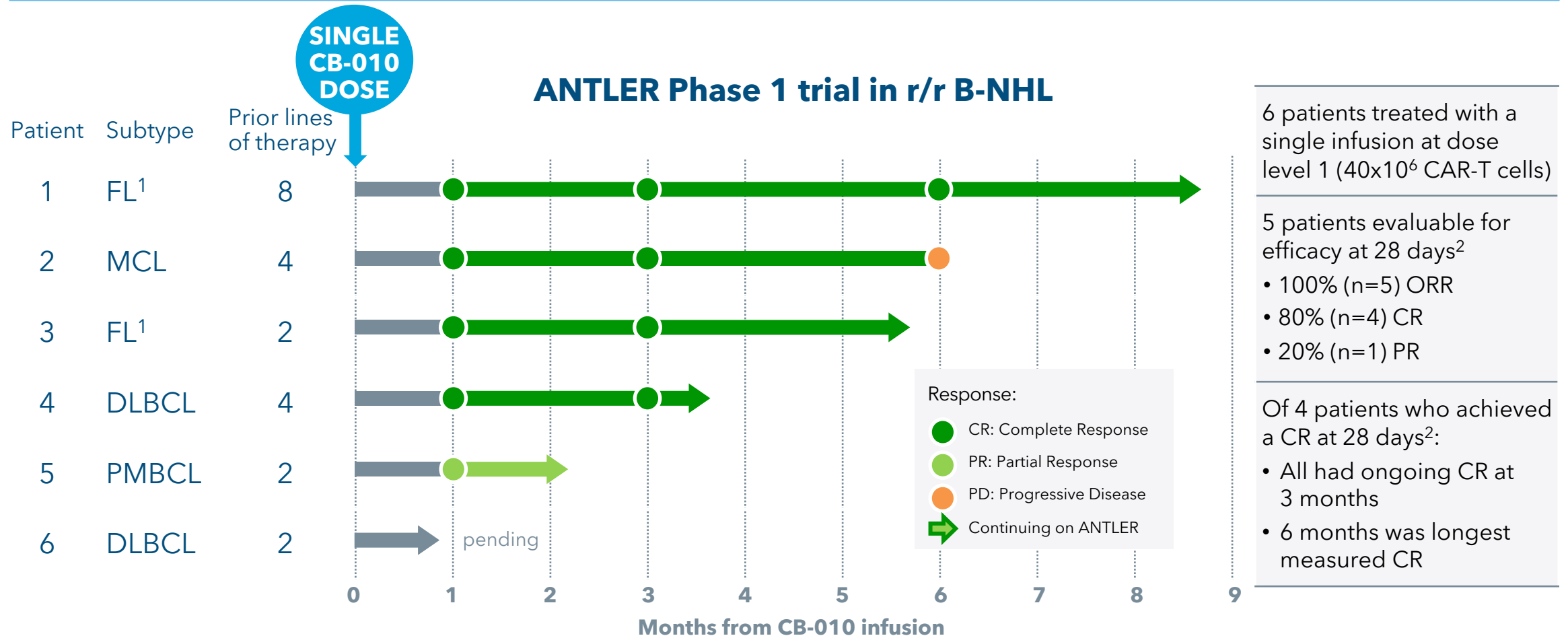
<sup>1</sup>As of February 23, 2022 data cutoff date, data collection ongoing

Source: Abstract for European Hematology Association (EHA) 2022 Hybrid Congress

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# CB-010: 1<sup>st</sup> allogeneic cell therapy to achieve 100% ORR



FL: follicular lymphoma MCL: mantle cell lymphoma DLBCL: diffuse large B cell lymphoma PMBCL: primary mediastinal large B cell lymphoma

<sup>1</sup> Aggressively behaving, with POD24 (high risk)

<sup>2</sup> As of February 23, 2022 data cutoff date, data collection ongoing, efficacy based on Lugano criteria

Source: Abstract for European Hematology Association (EHA) 2022 Hybrid Congress

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# Pipeline: initial focus on allogeneic cell therapy programs for solid and liquid tumors

Program	Target	Editing	Indications	Discovery	IND enabling	Phase 1	Phase 2	Phase 3 <sup>1</sup>	Anticipated milestone
<b>CAR-T platform with cell therapies for hematologic indications</b>									
CB-010	CD19	CAR into TRAC; armoring: PD-1 KO	r/r B-NHL	●	●	●	○	○	initial data scheduled for EHA
CB-011	BCMA	CAR into TRAC; armoring: B2M KO, B2M-HLA-E insertion	r/r MM	●	●	○	○	○	IND submission H2 2022
CB-012	CD371 <sup>2</sup>	CAR into TRAC; armoring: undisclosed	r/r AML	●	○	○	○	○	IND submission 2023
<b>CAR-NK platform with iPSC-derived cell therapies for solid tumor indications</b>									
CB-020	undisclosed	armoring: undisclosed	solid tumors	●	○	○	○	○	target selection Q4 2022
<b>AbbVie programs under collaboration agreement<sup>3</sup></b>									
CAR-T Program 1	undisclosed	undisclosed	undisclosed	●	○	○	○	○	
CAR-T Program 2	undisclosed	undisclosed	undisclosed	●	○	○	○	○	

<sup>1</sup> Phase 3 may not be required if Phase 2 is registrational

<sup>2</sup> Also known as CLL-1

<sup>3</sup> AbbVie has an option to include up to two additional CAR-T cell programs

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# Initial ANTLER data validate Caribou's chRDNA genome-editing platform

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- **100% ORR (80% CR) at 28 days<sup>1</sup> from a single dose of CB-010 at dose level 1 (N=5)  
1<sup>st</sup> allogeneic CAR-T cell therapy to achieve 100% ORR (5/5)  
Promising initial safety profile (N=6)**
- **Currently enrolling patients in ANTLER Phase 1 trial at dose level 2**
- **Longer duration data scheduled for EHA; additional data expected by YE 2022**
- **Goal to develop CB-010 as an allogeneic cell therapy that can meaningfully rival autologous cell therapies to reach broader groups of patients globally who need off-the-shelf cell therapy**
- **CB-010 is Caribou's lead program and part of a pipeline of precision genome-edited allogeneic CAR-T and CAR-NK cell therapies**
- **Experienced team and capital<sup>2</sup> to execute on our mission**

<sup>1</sup> As of February 23, 2022 data cutoff date, data collection ongoing, efficacy based on Lugano criteria

<sup>2</sup> \$391M in cash, cash equivalents, and marketable securities as of March 31, 2022

Source: Abstract for European Hematology Association (EHA) 2022 Hybrid Congress

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# With gratitude for patients, caregivers, investigators

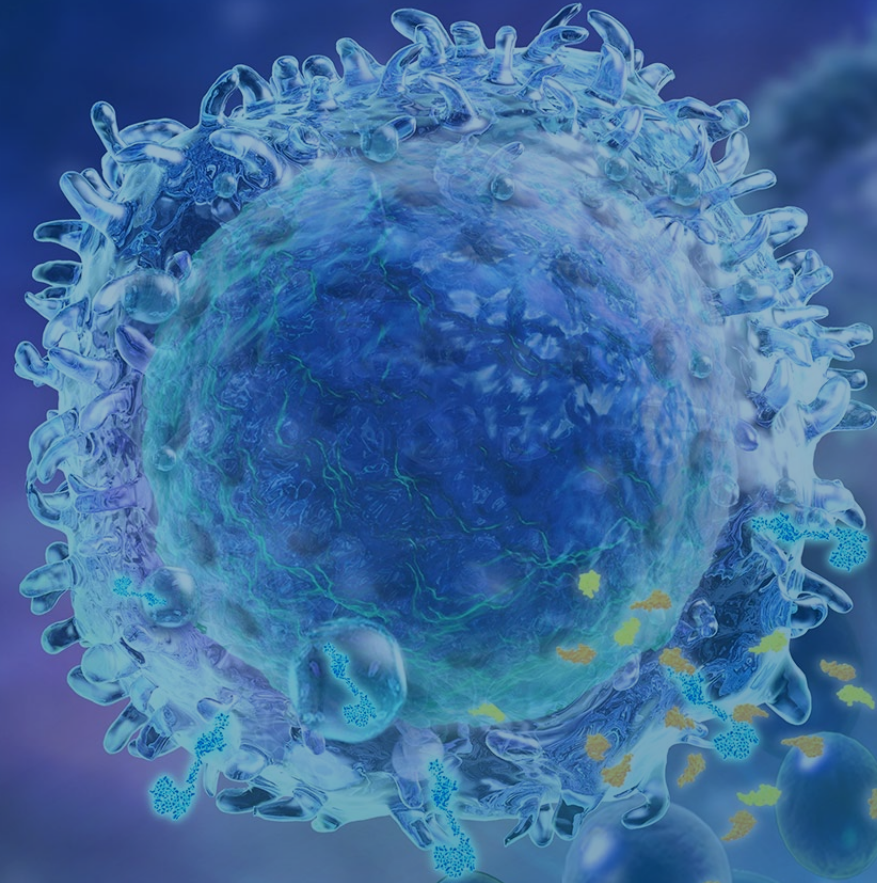
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- **MD Anderson Cancer Center, Houston**
- **Chao Family Comprehensive Cancer Center / University of California Irvine, Orange**
- **Oncology Hematology Care, Cincinnati**
- **Baylor Chares A. Sammons Cancer Center, Dallas**
- **HonorHealth, Scottsdale**
- **University of California San Diego Moores Cancer Center, La Jolla**
- **Additional sites coming soon**

## **THANK YOU**

for your contributions  
toward Caribou's mission  
to develop innovative,  
transformative therapies for  
patients with devastating  
diseases through novel  
genome editing

Q&A



# See you at EHA in June!



## Loretta J. Nastoupil, M.D.



Section Chief, New Drug Development  
Associate Professor, Department of  
Lymphoma/Myeloma

**The University of Texas MD Anderson  
Cancer Center**

### POSTER TITLE

First-in-human trial of CB-010, a CRISPR-edited allogeneic anti-CD19 CAR-T cell therapy with a PD-1 knock out, in patients with relapsed or refractory B cell non-Hodgkin lymphoma (ANTLER study) (Abstract P1455)

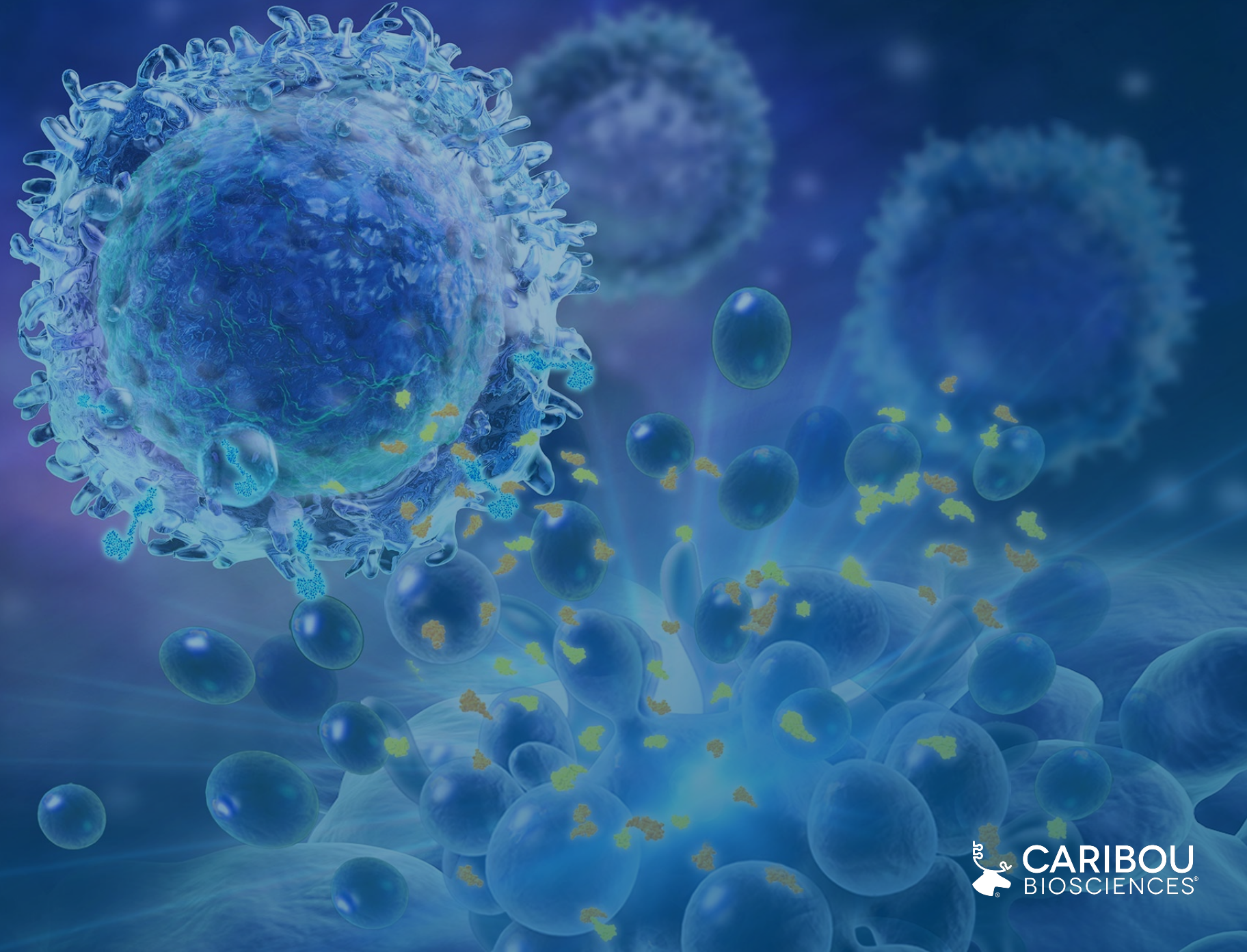
### DATE AND TIME

Friday, June 10, 2022  
16:30 - 17:45 CEST (10:30 - 11:45 am ET)

### SESSION TITLE

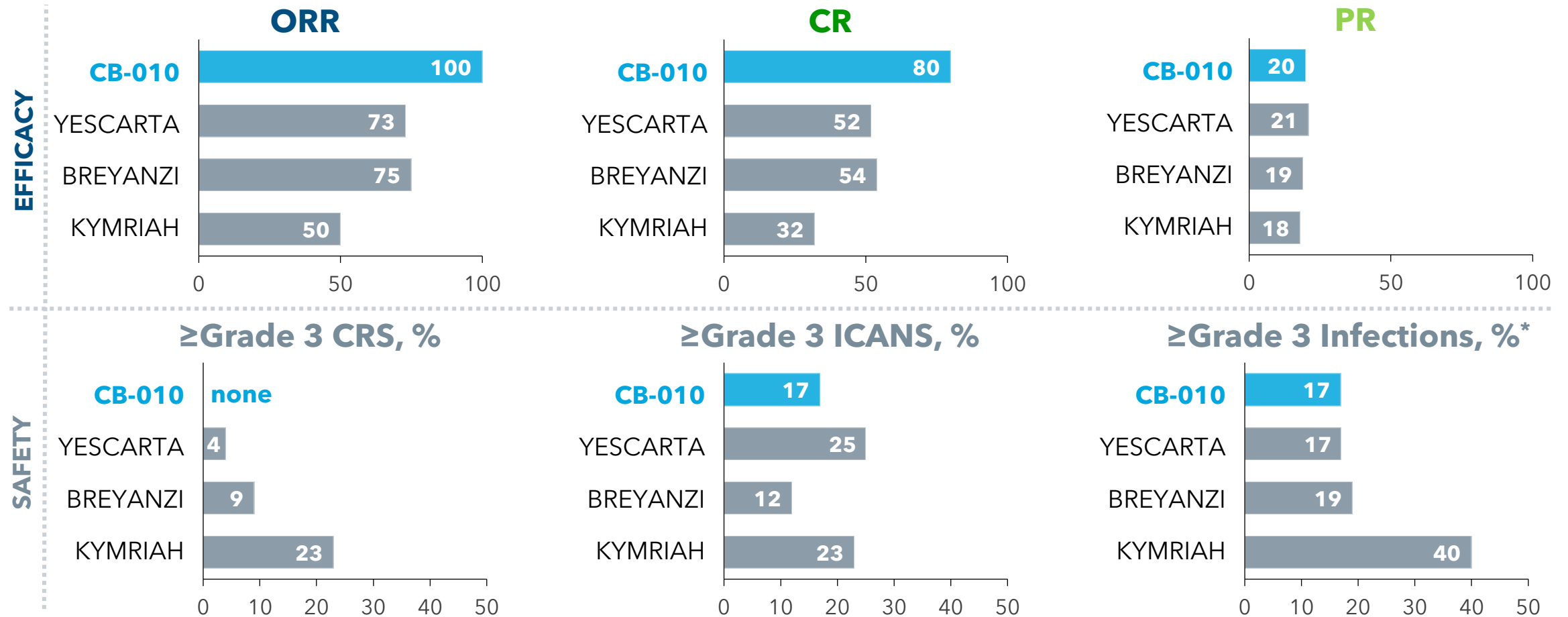
Gene therapy, cellular immunotherapy  
and vaccination - Clinical

# Appendix





# CB-010: an allogeneic cell therapy that may rival autologous anti-CD19 cell therapies



**CB-010:**  $40 \times 10^6$  CAR-T cells      **YESCARTA:**  $2 \times 10^6$  CAR-T cells/kg      **BREYANZI:** 50 to  $110 \times 10^6$  CAR-T cells      **KYMRIAH:**  $0.6$  to  $6.0 \times 10^8$  CAR-T cells

\* 1 patient with 2 ≥Grade 3 infections recorded prior to CB-010 infusion

Sources: package inserts for YESCARTA, BREYANZI, KYMRIAH

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# Deeper lymphodepletion protocol does not result in 100% ORR in B-NHL patients

## Clinical autologous CAR-T cell response rates following intensive LD regimens in B-NHL<sup>1</sup>

LD regimen prior to autologous anti-CD19 CAR-T cell therapy infusion	N=	Objective response rate (ORR)	Complete response (CR) rate
Cy 60 mg/kg/day + Flu 25 mg/kg <sup>2</sup> /day x 3-5 days	28	67%	42%

B-NHL: B cell non-Hodgkin lymphoma    Cy: cyclophosphamide    Flu: fludarabine    LD: lymphodepletion

<sup>1</sup> Turtle CJ et al. *Blood*. 2015;126(23):184

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# Thank you

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