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ANTLER initial clinical data for CB-010 at EHA 2022

June 10, 2022

Transformative genome-edited therapies for patients

Forward-looking statements

All statements in this presentation, other than statements of historical facts, are forward-looking statements, within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements speak only as of the date of this presentation and are subject to a number of known and unknown risks, assumptions, uncertainties, and other factors that may cause the actual results, levels of activity, performance, or achievements of Caribou Biosciences, Inc. (the "Company," "Caribou," "we," or "our") to be materially different from those expressed or implied by any forward-looking statements. The words "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential," or "continue" or the negative of these terms or other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. All statements other than statements of historical facts contained in this presentation, including but not limited to any statements regarding the initiation, timing, progress, strategy, plans, objectives, expectations, and results of our product candidate preclinical studies, clinical trials, and research programs, including our expectations and timing regarding the initial clinical data from our ANTLER phase 1 clinical trial for our CB-010 product candidate; our ability to successfully develop our product candidates and to obtain and maintain regulatory approval for our product candidates; the number and type of diseases, indications, or applications we intend to pursue; the beneficial characteristics, safety, efficacy, therapeutic effects, and potential advantages of our product candidates; the expected timing or likelihood of regulatory filings and approval for our product candidates; and the sufficiency and anticipated use of our existing capital resources to fund our future operating expenses and capital expenditure requirements and needs for additional financing are forward-looking statements. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date this presentation is given. This presentation discusses product candidates that are or will be under clinical investigation and that have not yet been approved for marketing by the U.S. Food and Drug Administration. No representation is made as to the safety or effectiveness of these product candidates for the therapeutic uses for which such product candidates are being or will be studied.

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.

In light of the foregoing, you are urged not to rely on any forward-looking statement or third-party data in reaching any conclusion or making any investment decision about any securities of the Company. The forward-looking statements in this presentation are made only as of the date hereof. Except to the extent required by law, the Company assumes no obligation and does not intend to update any of these forward-looking statements after the date of this presentation or to conform these statements to actual results or revised expectations.

This presentation shall not constitute an offer to sell or the solicitation of an offer to buy any securities.

Introduction

Rachel Haurwitz, PhD
President & CEO
Caribou Biosciences, Inc.

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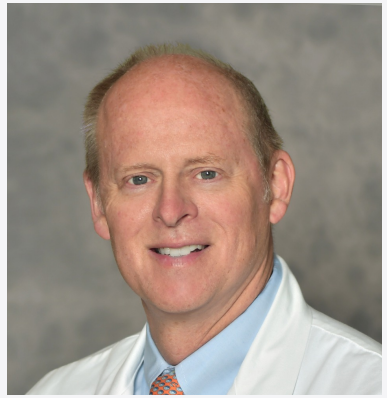
Today's guests

Loretta J. Nastoupil, MD

Section Chief, New Drug Development

Associate Professor, Department of Lymphoma/Myeloma

The University of Texas MD Anderson Cancer Center



James H. Essell, MD

OHC hematologist, medical oncologist, blood and marrow transplant specialist

Chair, Cellular Therapy, US Oncology Network

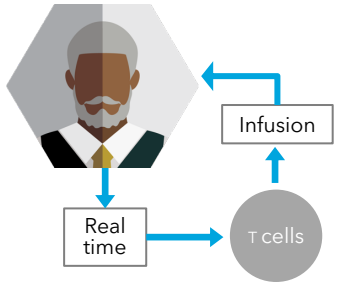
OHC – Specialists in Cancer and Blood Disorders

Aiming to set a new therapeutic bar for patients

Our mission is to develop innovative, transformative therapies for patients with devastating diseases through novel genome editing

Persistence is the key to unlocking the full potential of allogeneic cell therapies

Autologous therapy



Limited patient access
- Long vein-to-vein times
- Not all patients eligible
- Single dose

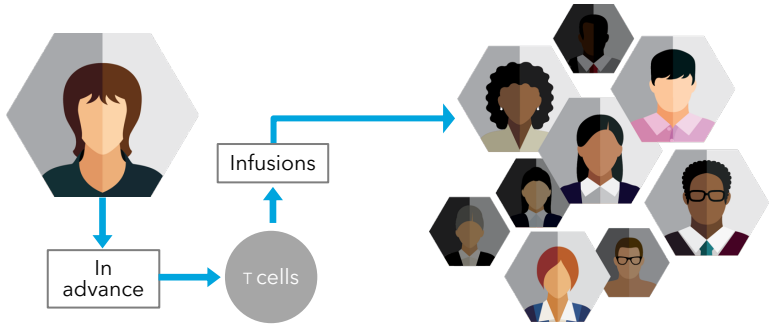
Bridging therapy often required

Manufacturing complexity

High production costs

Variable potency

Allogeneic therapy



Broad patient access
- Immediate availability
- Suitable for many patients
- Repeat dosing possible

Bridging therapy not required

Off-the-shelf availability

More efficient and cost-effective manufacturing

Healthy donor cells genome engineered for potency and persistence

… but efficacy remains a challenge
- Rapid rejection by immune system

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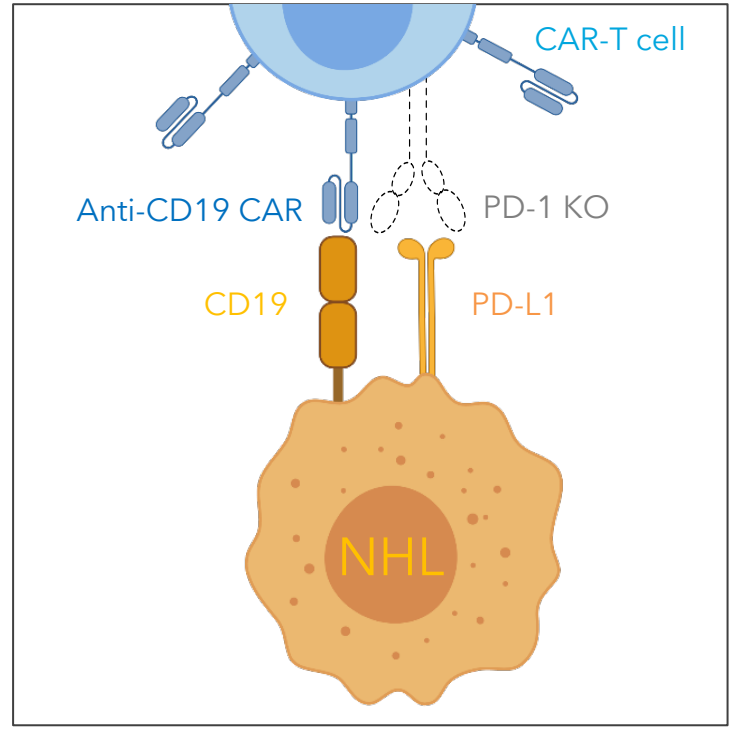
Persistence is the solution

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

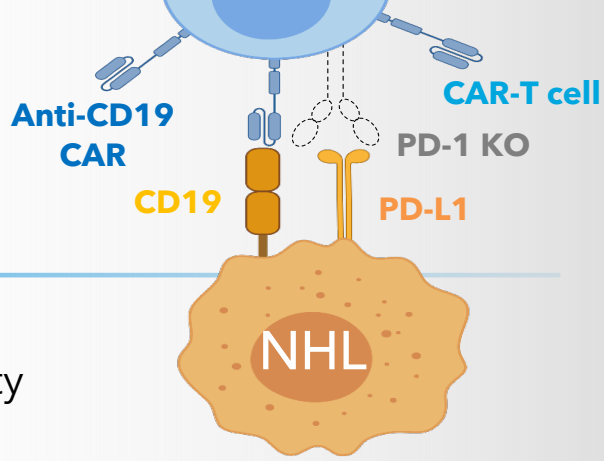
Key attributes	CB-010	Conventional allo anti-CD19 CAR-Ts
PD-1 KO for enhanced persistence of antitumor activity	✓	X
• Potentially better initial tumor debulking preclinically	✓	X
• Potentially better therapeutic index	✓	X
Site-specific insertion of CAR into *TRAC* locus	✓	Varies
• Eliminates random integration and reduces risk of GvHD		
Cas9 chRDNA editing for enhanced genomic integrity	✓	X
• Reduced off-target editing and genomic rearrangements	✓	X



Program: CB-010
Tumor antigen: CD19
Healthy donor leukapheresis-derived T cells
Indication: r/r non-Hodgkin lymphoma (NHL)
Status: Phase 1

Source: Caribou data on file

Our goal is to develop CB-010 as a transformative allogeneic cell therapy



- CB-010 is the **1st 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: 1st allogeneic CAR-T cell therapy to achieve a 100% CR

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

100% CR
6/6 patients

BEST RESPONSE

40% CR
2/5 patients

AT 6 MONTHS
(1 patient has not reached 6-month assessment)

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

Additional ANTLER data expected by YE 2022

Enrolling patients at dose level 2† → planning for future development

* $40x10^6$ CAR-T cells ; † $80x10^6$ CAR-T cells

[1] All data as of May 13, 2022 data cutoff date, data collection ongoing, efficacy measured by Lugano criteria

Source: Poster from European Hematology Association (EHA) 2022 Hybrid Congress

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With gratitude for patients, caregivers, investigators

- **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

Clinicaltrials.gov NCT#04637763

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ANTLER Phase 1 trial initial data for CB-010
EHA 2022

Loretta J. Nastoupil, MD

Section Chief, New Drug Development

Associate Professor, Department of Lymphoma/Myeloma

The University of Texas MD Anderson Cancer Center

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Disclosures

LJN has received honorarium for participation in advisory boards from ADC Therapeutics, BMS, Caribou Biosciences, Epizyme, Genentech/Roche, Genmab, Gilead/Kite, Janssen, MorphoSys, Novartis, and Takeda.

LJN has received research support from BMS, Caribou Biosciences, Epizyme, Genentech/Roche, Gilead/Kite, Janssen, IGM Biosciences, Novartis, and Takeda.

LJN serves on data safety monitoring boards for DeNovo, Genentech, MEI, and Takeda.

CB-010 ANTLER Phase 1 trial design

Patients with aggressive disease

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

Part A: 3+3 dose escalation
Objective: safety, determine MTD, RP2D

Part B: dose expansion
Objective: tumor response

r/r B-NHL

LYMPHODEPLETION

Cyclophosphamide
(60 mg/kg/d for 2 days)

Fludarabine
(25 mg/m2/d for 5 days)[2]

CB-010

DOSE LEVEL 1
40x10^6 CAR-T cells

SINGLE DOSE

- **Dose level 1**: 40x10^6 CAR-T cells (N=6, completed)
- **Dose level 2**: 80x10^6 CAR-T cells (enrolling patients)

-9 TO -2 DAYS | **0 DAYS** | **28 DAYS** | **3 MONTHS** | **6 MONTHS** | **9 MONTHS** | **12 MONTHS**

SAFETY AND TOLERABILITY

RESPONSE ASSESSMENT

MTD: maximum tolerated dose RP2D: recommended Phase 2 dose
[1] Aggressively behaving, with POD24 (high risk)
[2] Clin Cancer Res. 2011 July 1; 17(13): 4550–4557. doi:10.1158/1078-0432.CCR-11-0116
Clinicaltrials.gov NCT#04637763

ANTLER patients' baseline and disease characteristics

Characteristics	Cohort 1 (N=6)
Median age (range), years	65 (62-68)
Male, n (%)	5 (83)
ECOG performance status, n (%) 0 1	 5 (83) 1 (17)
Time since first diagnosis, years Median (range)	 6.0 (0.7-16)
Non-Hodgkin lymphoma subtype DLBCL FL[1] MCL PMBCL	 2 2 1 1
CD19+ disease, n (%)	6 (100)
Prior systemic therapies, median number (range)[2]	3 (2-8)

[1] Aggressively behaving, with POD24 (high risk)
[2] Patients are CD19 CAR-T naïve

Treatment emergent adverse events (TEAE)

Event Cohort 1 (N=6)	Any Grade[1] N (%)	Grade ≥ 3 N (%)	Related[2] Grade ≥ 3 N (%)
Total number of TEAEs	**137**	**39**	**17**
Patients with TEAEs	**6 (100)**	**5 (83)**	**4 (67)**
Neutropenia/neutrophil count decreased	5 (83)	5 (83)	1 (17)
Thrombocytopenia/platelet count decreased	4 (67)	4 (67)	3 (50)
Anemia	4 (67)	2 (33)	-
White blood cell count decreased	3 (50)	3 (50)	3 (50)
Lymphocyte count decreased	3 (50)	2 (33)	1 (17)
Lactate dehydrogenase (LDH) increased	2 (33)	1 (17)	1 (17)
Cytokine release syndrome (CRS)	2 (33)	-	-
Blood creatinine increased	2 (33)	-	-
Fatigue	2 (33)	-	-
Hypoalbuminemia	2 (33)	-	-
Hypocalcemia	2 (33)	-	-
Hyponatremia	2 (33)	-	-
ICANS	1 (17)	1 (17)	1 (17)
Febrile neutropenia	1 (17)	1 (17)	-
Syncope	1 (17)	1 (17)	-

[1] TEAE in at least 2 patients of any grade or TEAE in at least 1 patient of Grade ≥ 3 are included
[2] Related TEAEs include TEAEs with relationship to CB-010 of "probably related" or "related" as evaluated by investigator
As of May 13, 2022 data cutoff date

AEs of special interest

Event	Cohort 1 (N=6)
CRS[1], n (%)	
Any grade	2 (33)
Grade 1	2 (33)
Grade ≥ 2	0 (0)
Median time to onset, days (range)	4 (1-7)
Median duration of events, days (range)	8 (7-8)

[1]1 CRS required treatment. Patient received tocilizumab (8mg x 2) and antibiotics and was hospitalized

Event	Cohort 1 (N=6)
ICANS[2], n (%)	
Any grade	1 (17)
Grade 3	1 (17)
Grade ≥ 4	0 (0)
Time to onset, days	8
Duration of event, days	<2 (~39 hrs)

[2] Patient received dexamethasone (10mg x 2 and 20mg x 4) and was hospitalized

Event	Cohort 1 (N=6)
Infections[3], n (%)	
Any grade	2 (33)
Grade 1	0 (0)
Grade 2	1 (17)
Grade 3	1 (17)
Median time to onset, days (range)	8.5 (2-140)
Median duration of events, days (range)	5 (1-56)

[3] Grade 3, pre-CB-010 infusion. Grade 2, post-CB-010 infusion. None were related to CB-010

As of May 13, 2022 data cutoff date

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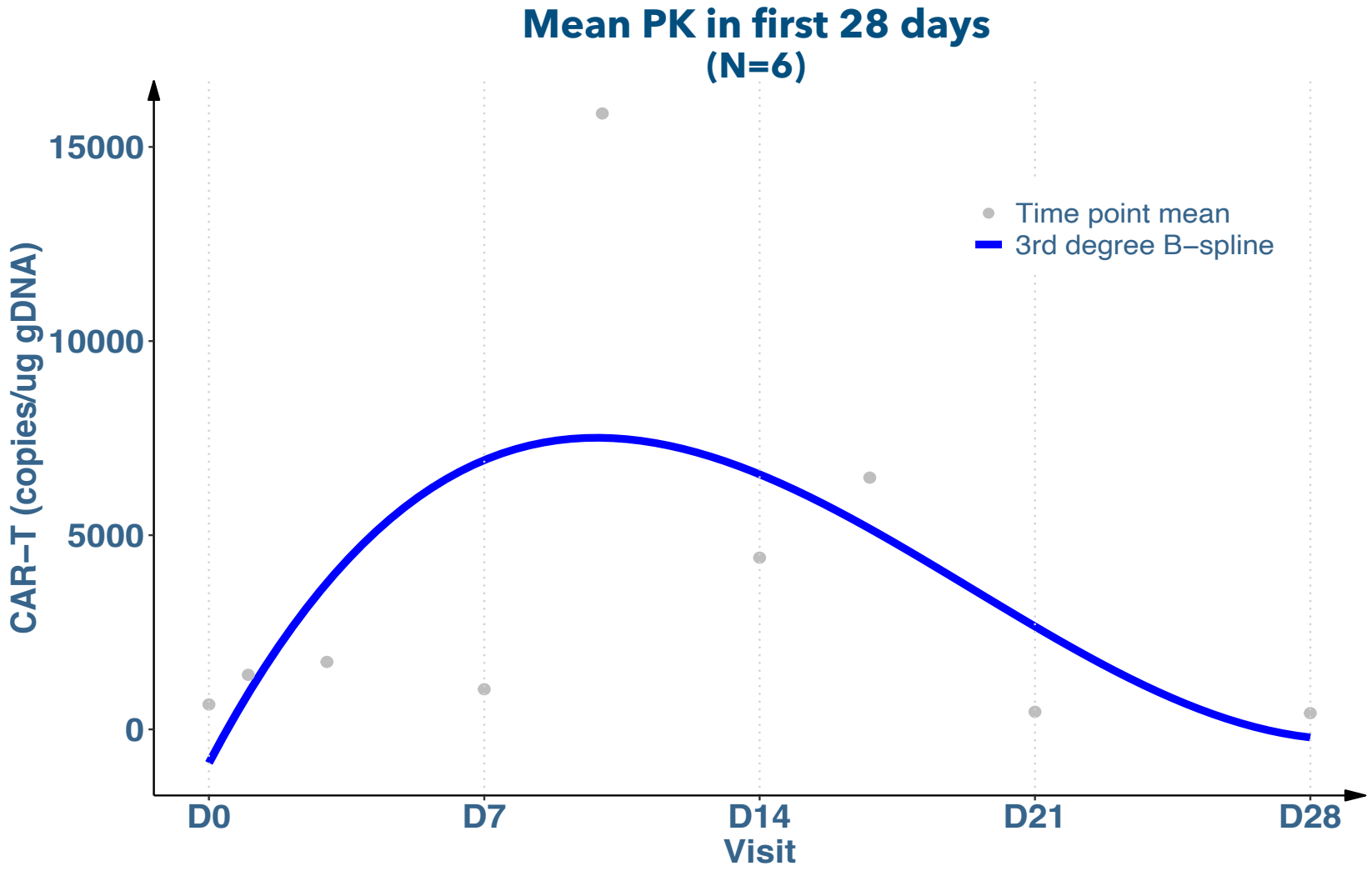
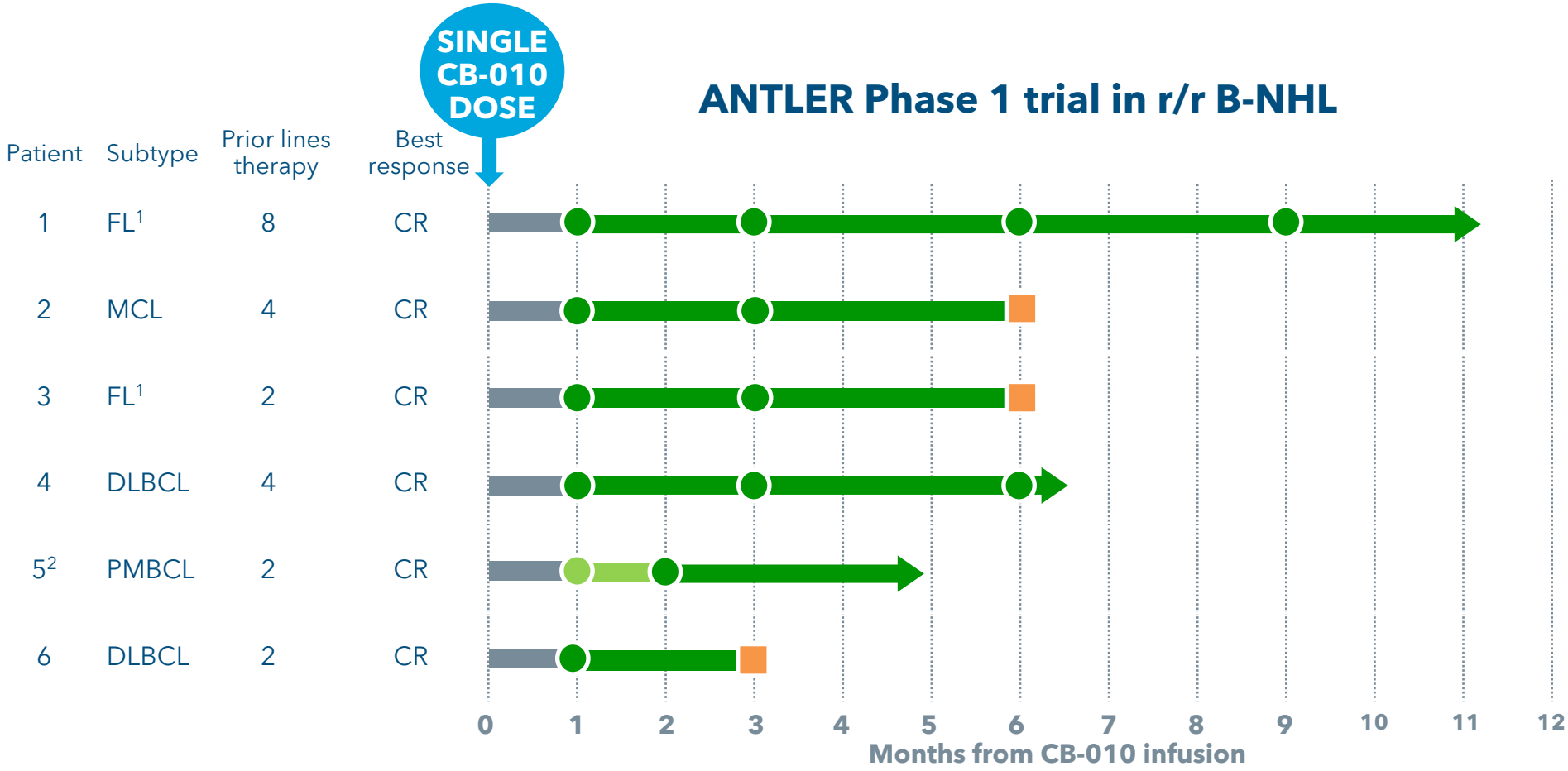
Kinetics of CB-010



CB-010: preliminary efficacy



6 patients treated with a single infusion at dose level 1 ($40x10^6$ CAR-T cells)

6 patients evaluable for efficacy[3]
- 100% CR (6/6, best response)
- 40% CR (2/5) at 6 months

9 months was longest measured CR

CRs measured by investigator assessment and central read

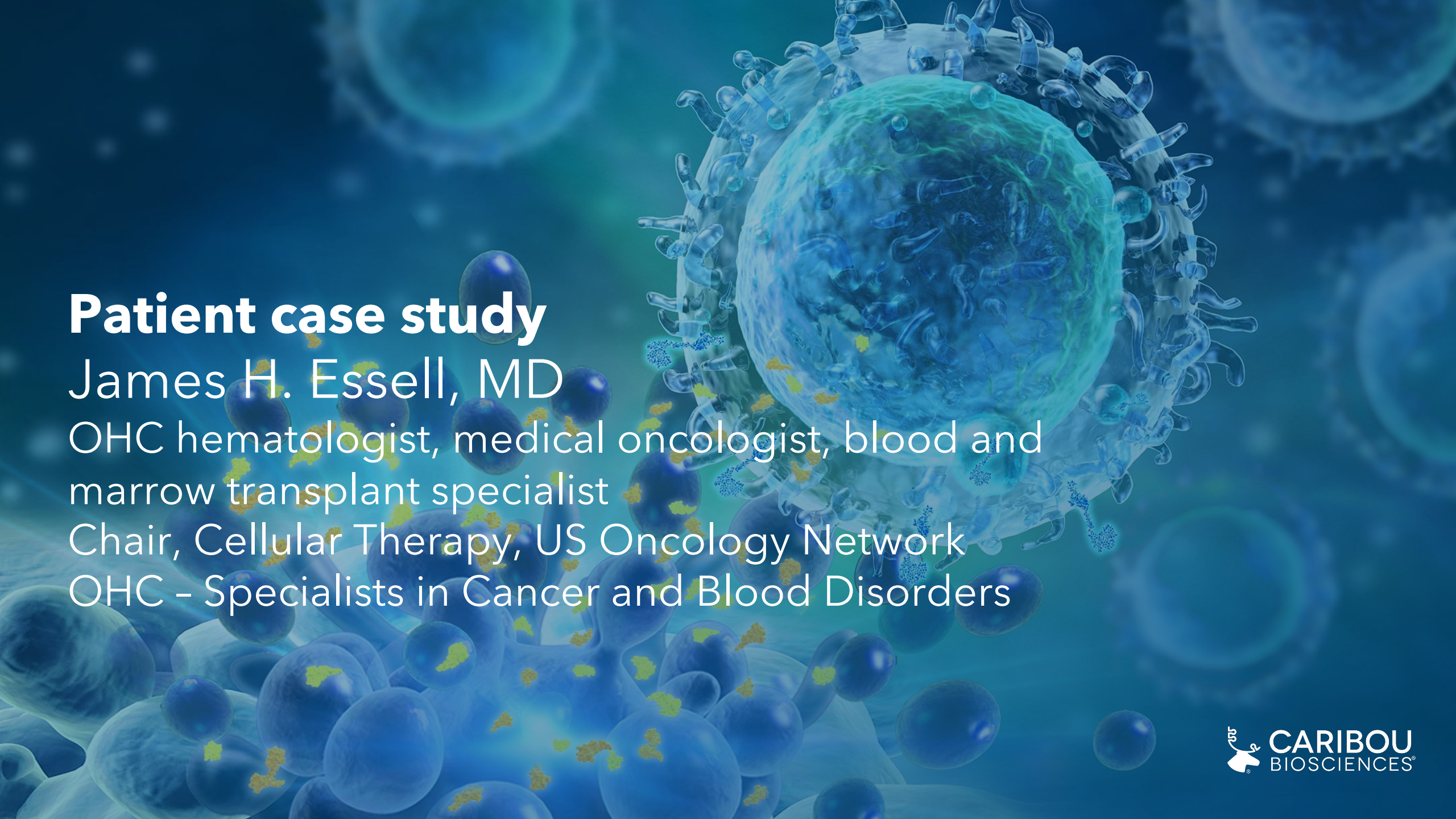
Response:
- CR: Complete Response
- PR: Partial Response
- PD: Progressive Disease
- Continuing on ANTLER

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

[1] Aggressively behaving, with POD24 (high risk)

[2] Patient 5's 3-month scan conducted on day 63 post CB-010 as per investigator's discretion

[3] As of May 13, 2022 data cutoff date, data collection ongoing, efficacy based on Lugano criteria



Patient case study

James H. Essell, MD
OHC hematologist, medical oncologist, blood and marrow transplant specialist
Chair, Cellular Therapy, US Oncology Network
OHC – Specialists in Cancer and Blood Disorders

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CASE STUDY
ANTLER Phase 1 trial

Patient #1[1]

Age: 66

Gender: M

BMI: 25.4

Original prognosis

Tumor subtype: FL (aggressively behaving, with POD24)

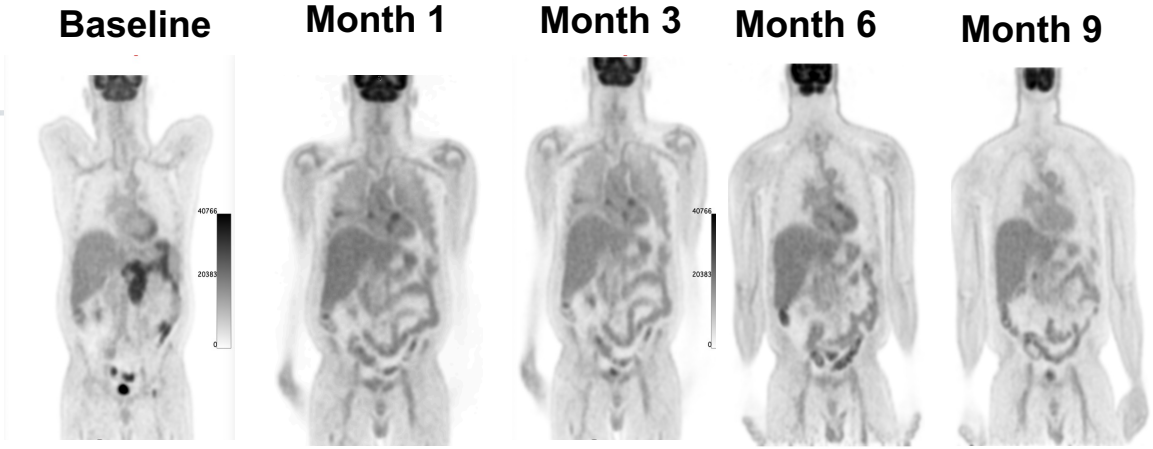
Stage: IV

Years since diagnosis: 8

Lines of prior therapy: 8

History: multiple relapses and progressive disease, then enrolled on ANTLER trial

PET-CT scans[2]



Significant disease burden with 10 cm abdominal mass

CR **CR** **CR** **CR**

After CB-010 dose level 1 treatment[3]

Days since CB-010 infusion: 329

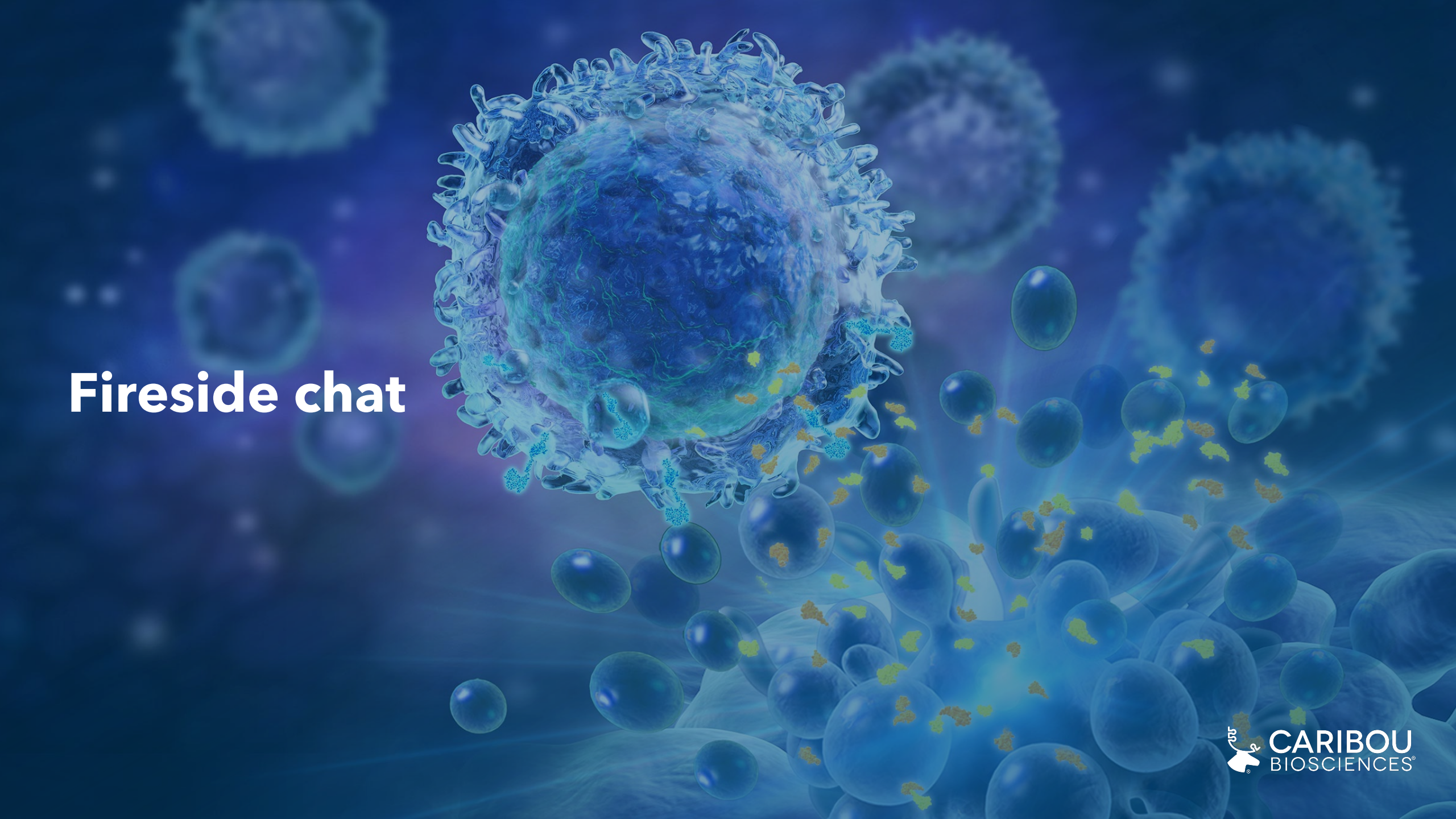
Best ORR: confirmed CR from Day 28 post-infusion to Month 9

Tolerability: Grade ≥ 3 related AE: 1

Status: continuing on study

[1] The information presented in this patient case study relates to one patient and may not be reflective of any of the other patients in the ANTLER Phase 1 trial. In addition, initial or interim clinical trial data is subject to the risk that it will not ultimately be predictive of the safety and efficacy of the product candidates and that clinical outcomes may differ as more and longer-term clinical data become available.
[2] Responses evaluated by investigator assessment and independent radiologist
[3] As of May 13, 2022 data cutoff date, data collection ongoing, efficacy based on Lugano criteria

Fireside chat



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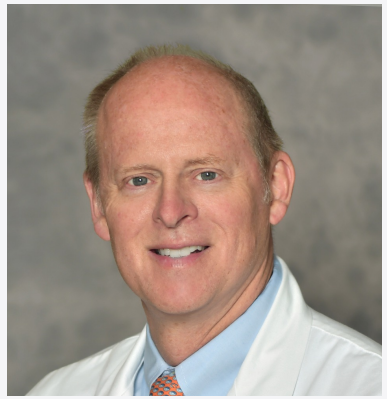
Fireside chat with Dr. Nastoupil and Dr. Essell

Loretta J. Nastoupil, MD

Section Chief, New Drug Development

Associate Professor, Department of Lymphoma/Myeloma

The University of Texas MD Anderson Cancer Center



James H. Essell, MD

OHC hematologist, medical oncologist, blood and marrow transplant specialist

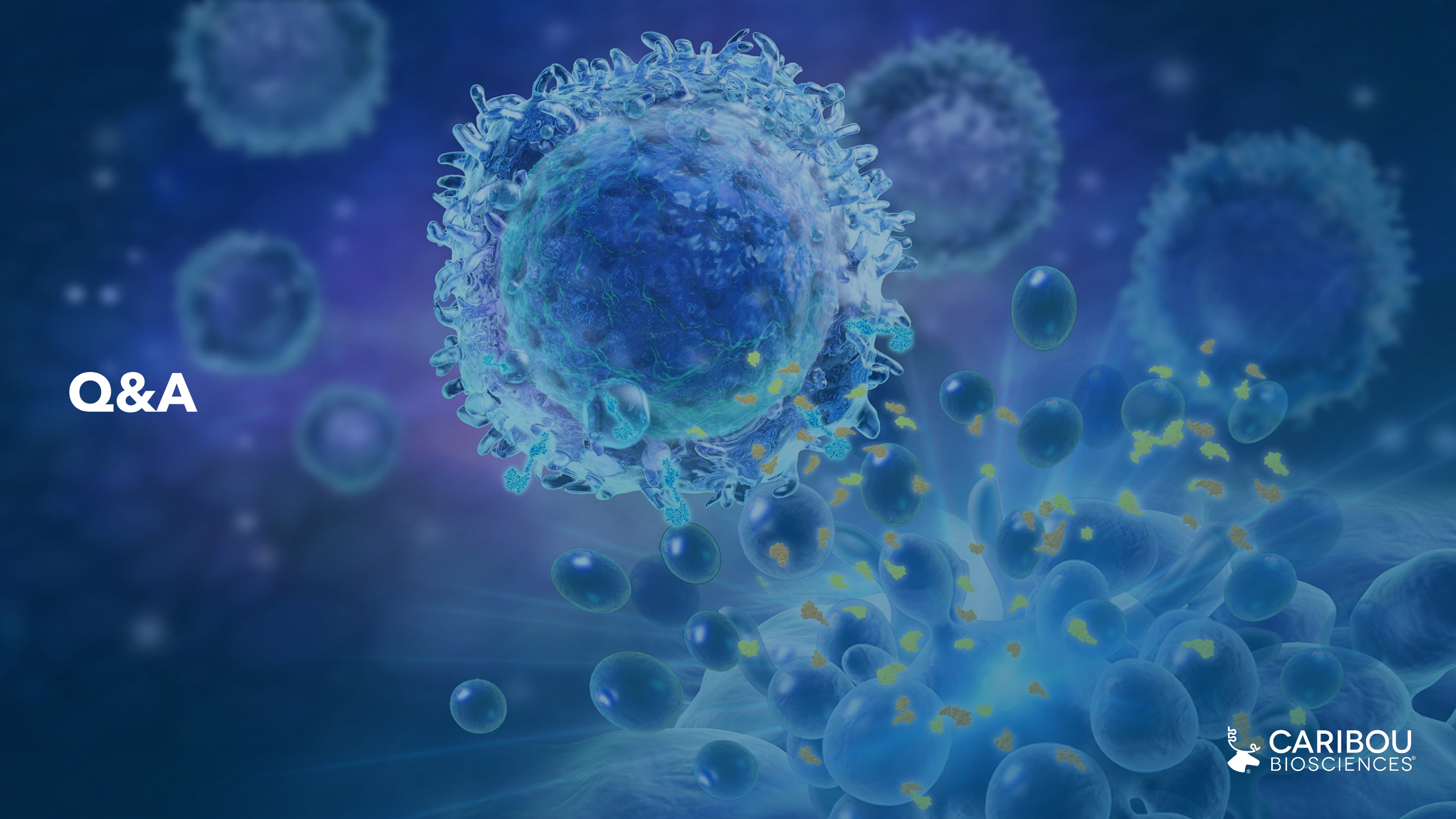
Chair, Cellular Therapy, US Oncology Network

OHC – Specialists in Cancer and Blood Disorders

Rachel Haurwitz, PhD
President and CEO

Caribou Biosciences

Q&A



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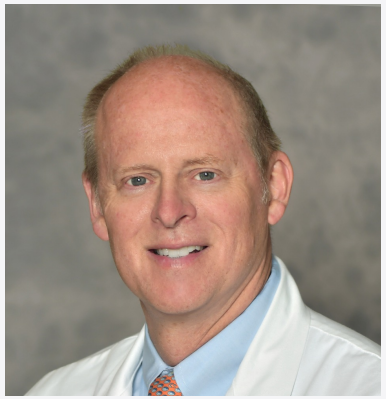
Open to your questions

Loretta J. Nastoupil, MD

Section Chief, New Drug Development

Associate Professor, Department of Lymphoma/Myeloma

The University of Texas MD Anderson Cancer Center



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OHC – Specialists in Cancer and Blood Disorders

Rachel Haurwitz, PhD
President and CEO
Director

Caribou Biosciences

Syed Rizvi, MD
Chief Medical Officer

Caribou Biosciences

Steve Kanner, PhD
Chief Scientific Officer

Caribou Biosciences

Closing remarks

Rachel Haurwitz, PhD
President & CEO
Caribou Biosciences, Inc.

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Initial ANTLER data are an important step toward validating Caribou's chRDNA genome-editing platform

- **100% CR rate[1] (6/6, best response), 40% CR rate[1] (2/5) at 6 months from a single dose of CB-010 at dose level 1**
  1st allogeneic CAR-T cell therapy to achieve 100% CR rate, best response
  Promising initial safety profile
- **Currently enrolling patients in ANTLER Phase 1 trial at dose level 2**
- **Additional ANTLER 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[2] to execute on our mission**

[1] As of May 13, 2022 data cutoff date, data collection ongoing, efficacy based on Lugano criteria
[2] $391M in cash, cash equivalents, and marketable securities as of March 31, 2022

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

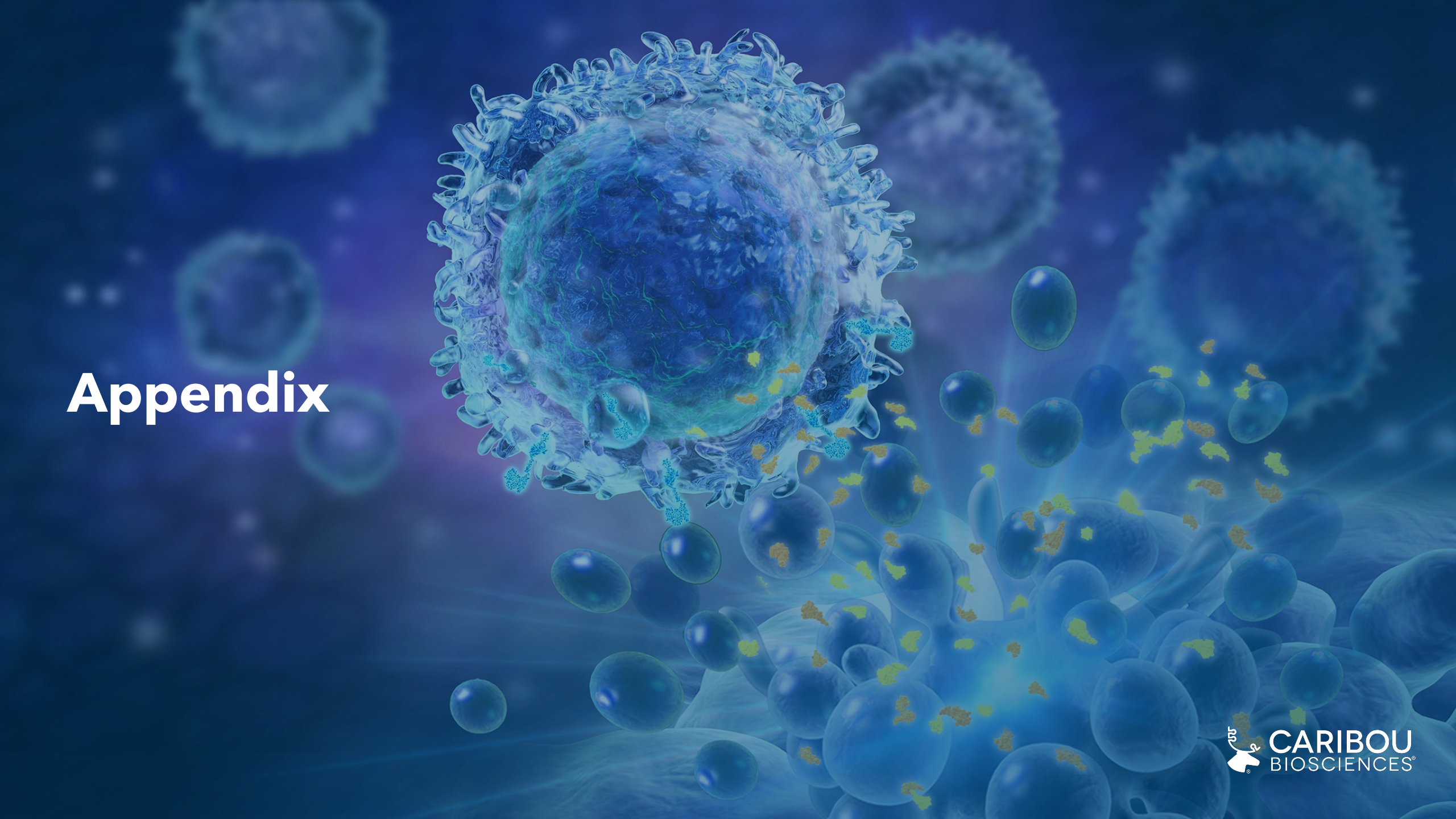
Program	Target	Editing	Indications	Discovery	IND enabling	Phase 1	Phase 2	Phase 3[1]	Anticipated milestone
CAR-T platform with cell therapies for hematologic indications									
CB-010	CD19	CAR into TRAC; armoring: PD-1 KO	r/r B-NHL	●	●	●	○	○	Additional data expected YE 2022
CB-011	BCMA	CAR into TRAC;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

[1] Phase 3 may not be required if Phase 2 is registrational
[2] Also known as CLL-1
[3] AbbVie has an option to include up to two additional CAR-T cell programs

Thank you

cariboubio.com
info@cariboubio.com

Appendix



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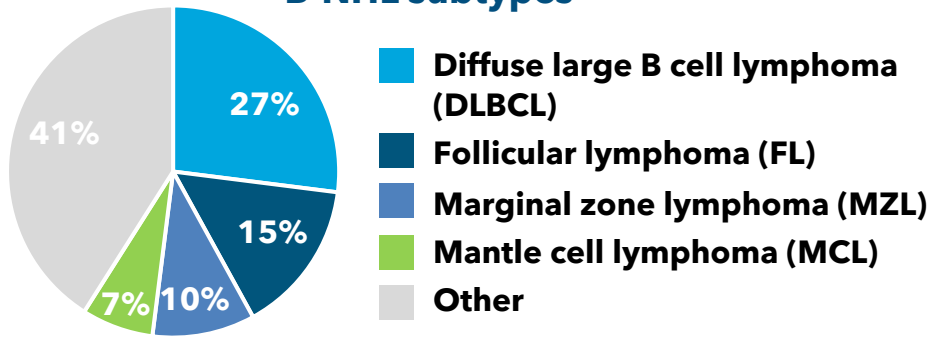
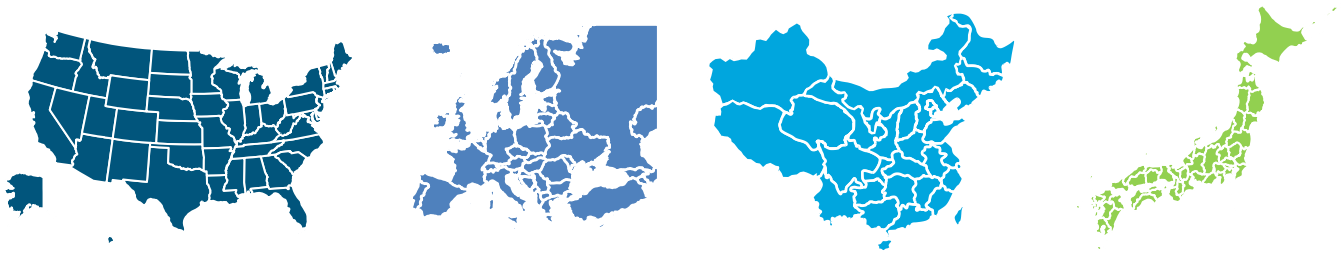
r/r B-NHL: high unmet need globally for off-the-shelf cell therapy

- 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)[1]
- Current autologous CAR-T cell therapies have limited patient access with complex manufacturing and high production costs

B-NHL subtypes[1]



Worldwide NHL incidence[2]



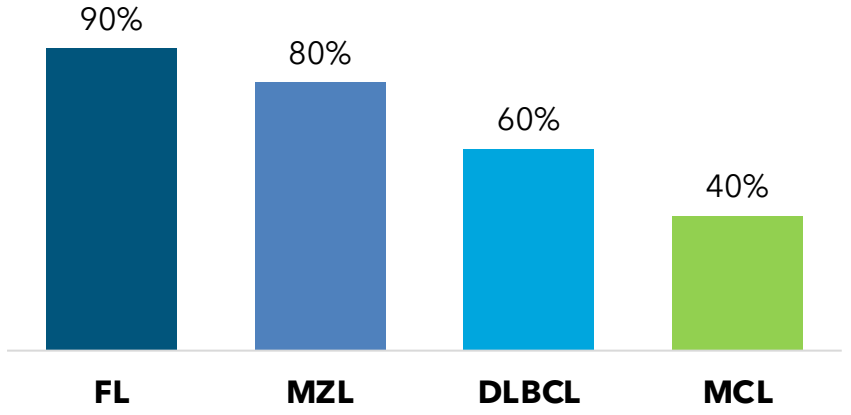
US incidence[1]: ~82,900

EU incidence: ~101,000

China incidence: ~97,500

Japan incidence: ~33,600

B-NHL 5-year post-diagnosis survival rates[3]



[1] National Cancer Institute, Leukemia & Lymphoma Society, Lymphoma Research Foundation
[2] Evaluate Pharma, May 2022, www.evaluate.com
[3] Cancer Research U.K.

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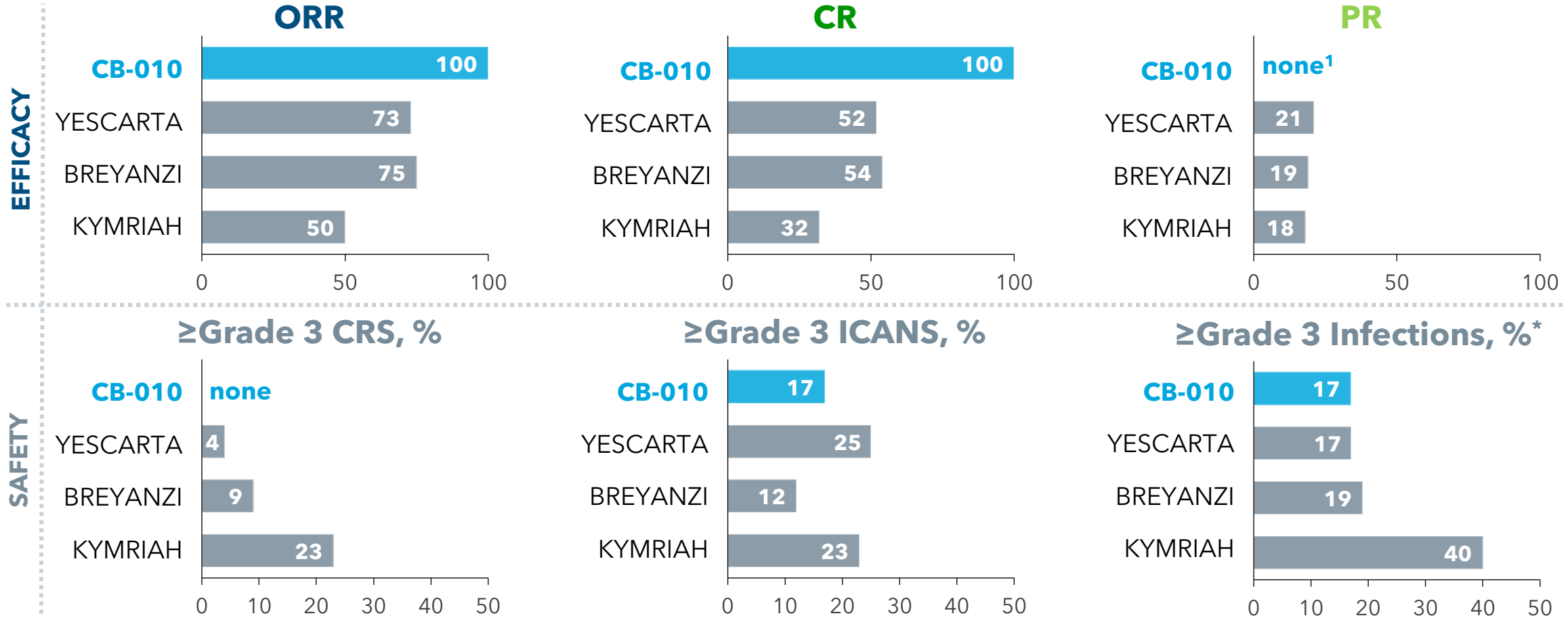
CB-010: an allogeneic cell therapy that may rival autologous anti-CD19 cell therapies



CB-010: 40x10^6 CAR-T cells **YESCARTA:** 2x10^6 CAR-T cells/kg **BREYANZI:** 50 to 110x10^6 CAR-T cells **KYMRIAH:** 0.6 to 6.0x10^8 CAR-T cells

[1] Patient 5 who had PR at Day 28 converted to CR at Day 63
* 1 patient with 2 Grade 3 infections recorded prior to CB-010 infusion
Sources: package inserts for YESCARTA, BREYANZI, KYMRIAH

Information regarding competitors and their results may be based on different stages of trials, different trial designs, and may be based on different assumptions or estimates. Caution should be used when evaluating competitor results presented against CB-010 and the reader should not place undue reliance on this comparative information.

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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[1]

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^2/day x 3-5 days	28	67%	42%

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

[1] Turtle CJ et al. *Blood.* 2015;126(23):184

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