CARIBOU BIOSCIENCES®

Corporate Presentation

March 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, and results of our product candidate preclinical studies, clinical trials, and research programs; 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; our ability to identify additional products, product candidates, or technologies with significant commercial potential that are consistent with our commercial objectives; 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 financial position and our ability to raise additional capital as needed to fund our operations and product candidate development; risks associated with the initiation, cost, timing, progress, and results of current and future research and development programs, preclinical studies, and clinical trials; 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 on our business and operations; and other risks are described in greater detail in the section titled "Risk Factors" of our final prospectus filed with the Securities and Exchange Commission on July 23, 2021 pursuant to Rule 424(b)(4) of the Securities Act of 1933, as amended, and other filings we make with the Securities and Exchange Commission, 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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This presentation shall not constitute an offer to sell or the solicitation of an offer to buy any securities.


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

Caribou's approach: precision genome editing

chRDNA genome-editing platform

- Genome-editing platform with superior specificity
  - Precision next-generation chRDNA technology
  - Highly specific multiplex edits while maintaining genomic integrity
- Broad potential therapeutic applications, including oncology and beyond

Robust pipeline of allogeneic CAR-Ts & CAR-NKs

- Initial focus on allogeneic CAR-T and CAR-NK cell therapies for broad patient access
- Genome editing for enhanced persistence of anti-tumor activity
- 4 wholly-owned allogeneic cell therapies for hematologic and solid tumors
- CB-010 in Phase 1 ANTLER study in r/r B-NHL, initial data expected in 2022
- 2 CAR-T cell therapy programs for AbbVie under strategic collaboration

Strong foundation for execution

- CRISPR pioneers, including Nobel Prize winner Jennifer Doudna, co-founded Caribou
- Experienced, expanded leadership
- 53 issued U.S. patents, including 8 U.S. patents covering chRDNA technology[1]
- $435M in cash[2], including $321M in net IPO proceeds in Q321

[1] Patent data as of March 1, 2022
[2] Cash and cash equivalents as of September 30, 2021

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Caribou's proprietary technologies offer broad applications to enable transformational therapies

Initial focus: allogeneic cell therapies

Improved persistence through diverse strategies

- CB-010: anti-CD19 CAR-T cells with PD-1 knockout
- CB-011: anti-BCMA CAR-T cells with immune cloaking
- Pipeline of CAR-T, CAR-NK, AbbVie programs under collaboration

Future potential applications:

Ex vivo

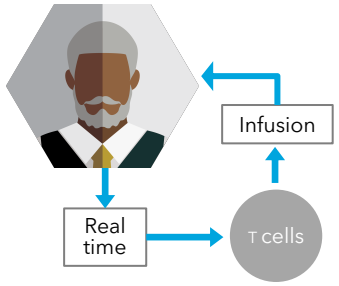
- Leverage the power of precision cell therapies into disease areas **beyond oncology**
- Expand engineered iPSC-derived therapies **beyond NK cells**

In vivo

- Apply the Cas12a chRDNA platform to ***in vivo*** **applications**

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

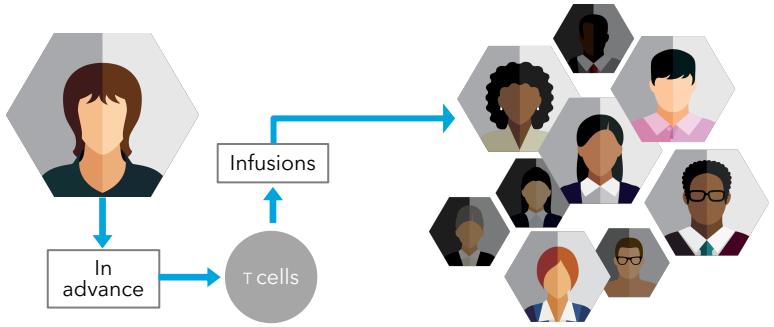
Bridging therapy often required

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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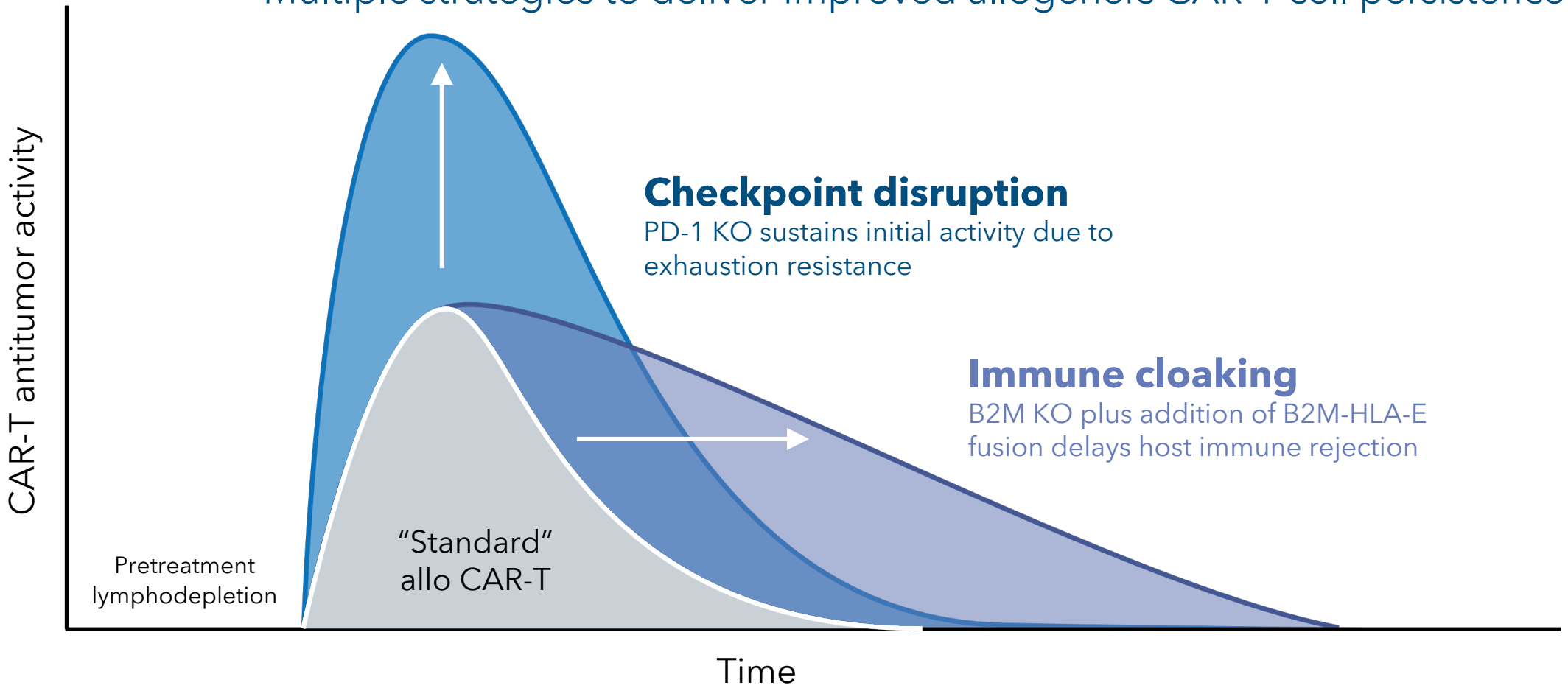
Persistence is the solution

Caribou's approach: armor cell therapies to increase the persistence of antitumor activity

Multiple strategies to deliver improved allogeneic CAR-T cell persistence



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	●	●	●	○	○	initial data expected 2022
CB-011	BCMA	CAR into TRAC; armoring: B2M KO, B2M-HLA-E insertion	r/r MM	●	●	○	○	○	IND filing 2022
CB-012	CD371	CAR into TRAC; armoring: undisclosed	r/r AML	●	○	○	○	○	IND filing 2023
CAR-NK platform with iPSC-derived cell therapies for solid tumor indications									
CB-020	undisclosed	armoring: undisclosed	solid tumors	●	○	○	○	○	target selection 2022
AbbVie programs under collaboration agreement[2]									
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] AbbVie has option to include up to two additional CAR-T cell programs

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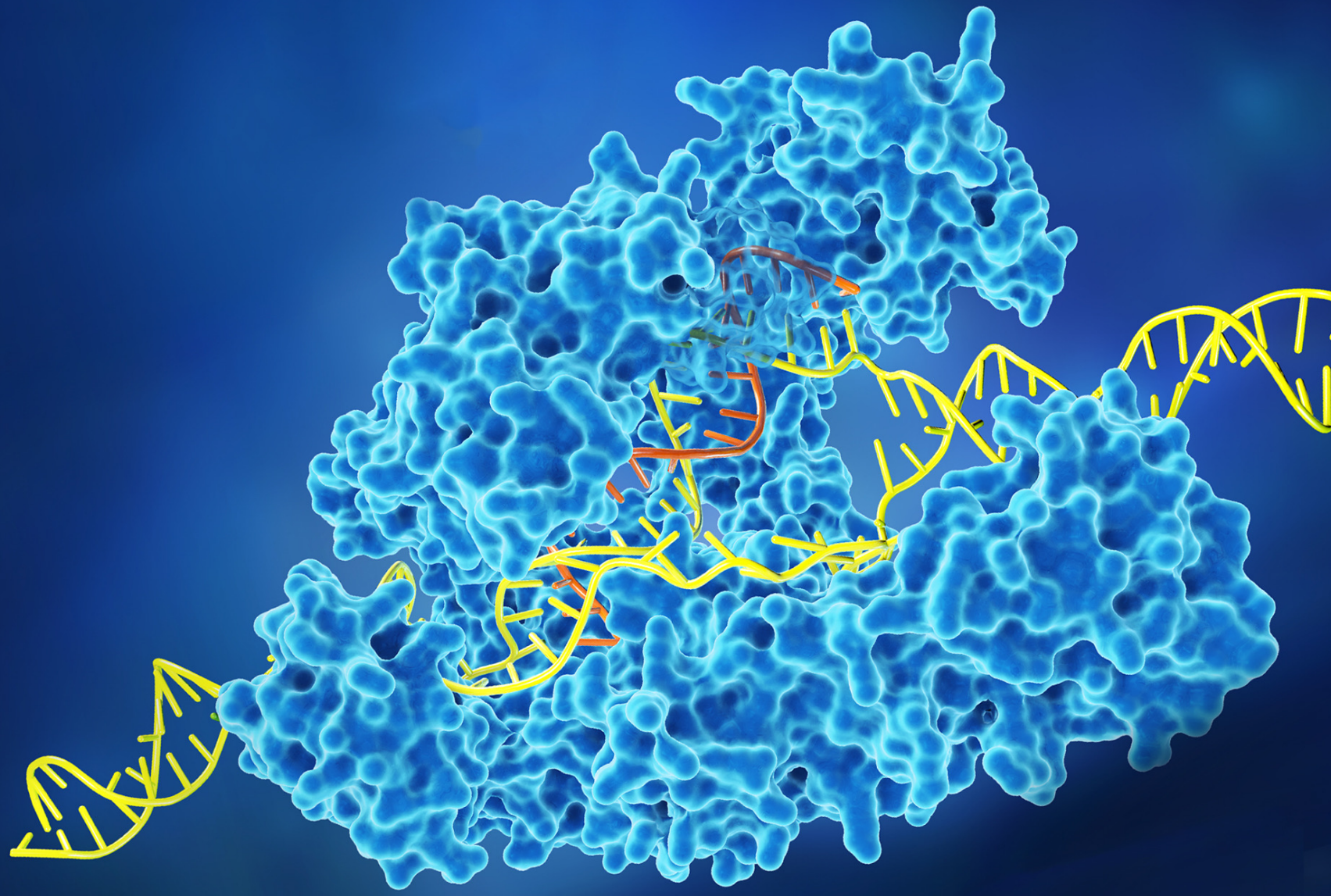
Our chRDNA platform



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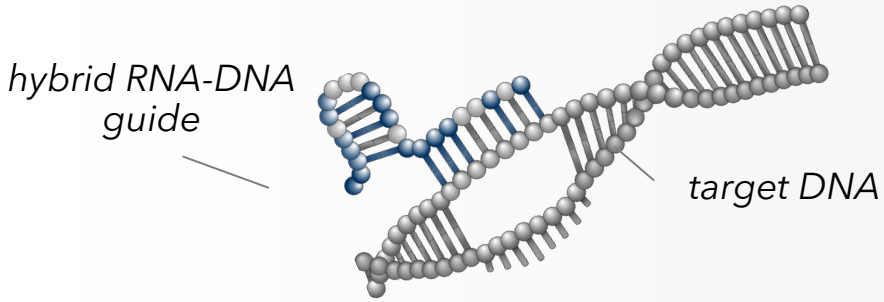
chRDNA: a proprietary CRISPR platform with significant advantages over 1st gen CRISPR-Cas9

Significantly improved genome-editing specificity	• Substantially fewer off-target events compared to first generation CRISPR-Cas9
High efficiency gene knockouts and insertions	• Enables robust multiplex editing with high genomic integrity
Versatility across a broad range of cell types	• Sophisticated genome editing across many cell types including immune cells and stem cells
Simple chemical synthesis	• chRDNA guides are manufactured via chemical synthesis using readily available technologies

Combining powerful technologies to create sophisticated allogeneic cell therapies

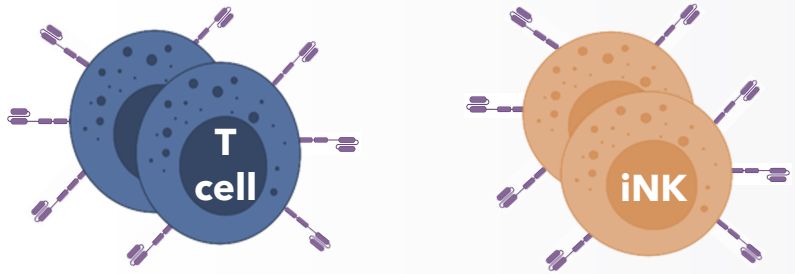
chRDNA editing platform

CRISPR hybrid RNA-DNA guides



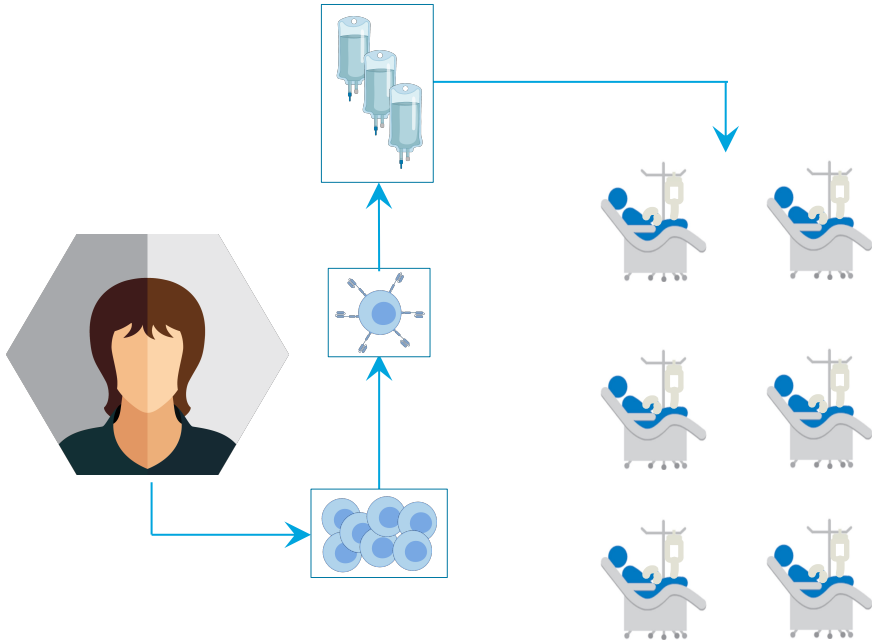
CAR-modified immune cells

Healthy donor T cells or iPSC-derived NK cells



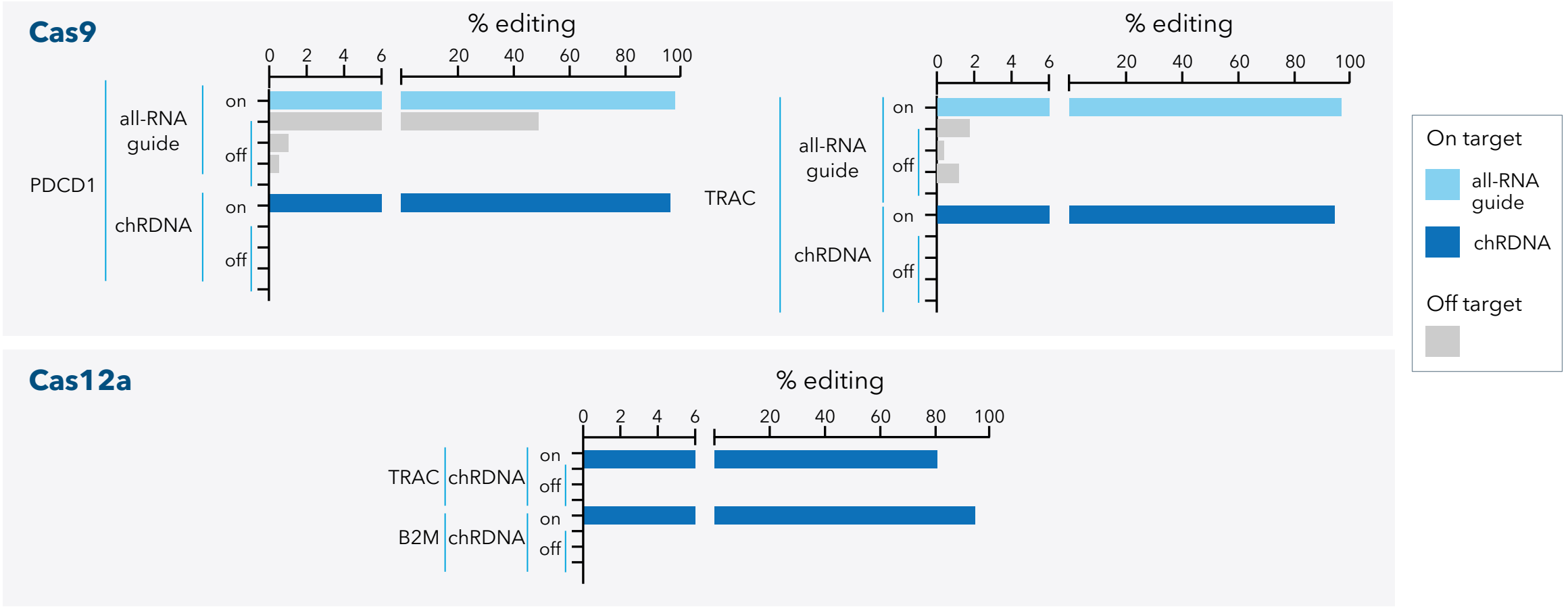
Allogeneic multiplex-edited immune cell therapies

Edited to deliver extended *persistence*



chRDNA guides significantly improve editing specificity

Human primary T cell editing data



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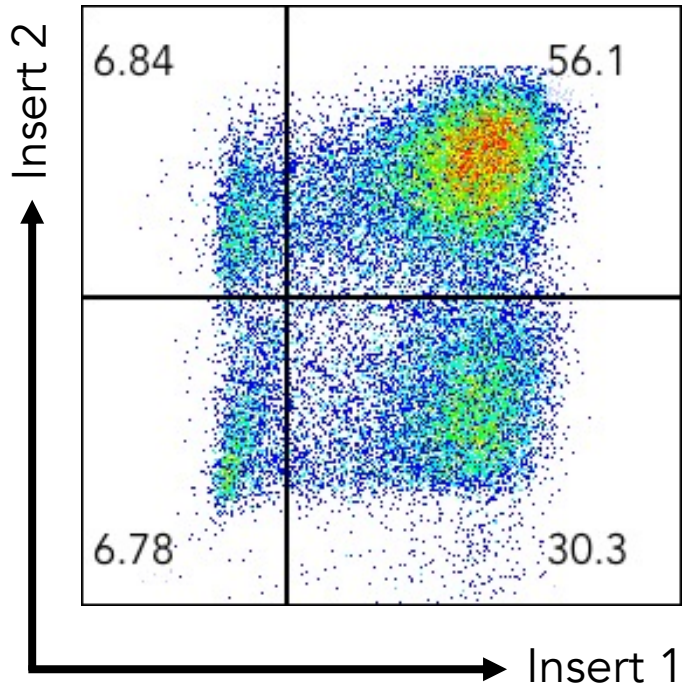
Cas12a chRDNAs drive exceptionally high insertion efficiencies

Cas12a chRDNAs mediate high-level insertion rates in primary T cells

- High efficiency site-specific insertions remain a key bottleneck for genome editing
- Cas12a chRDNAs drive high efficiency gene insertions, enabling insertion of multiple genes for highly sophisticated cell therapies
  - Caribou delivers the donor gene of interest via AAV6 transduction of T cells
  - Cas12a chRDNA editing yields site-specific insertion of the donor gene

High efficiency Cas12a chRDNA editing yields >50% of the modified T cells possessing all 4 intended edits[1]



[1]Data generated by Caribou PD using representative CB-011 manufacturing process

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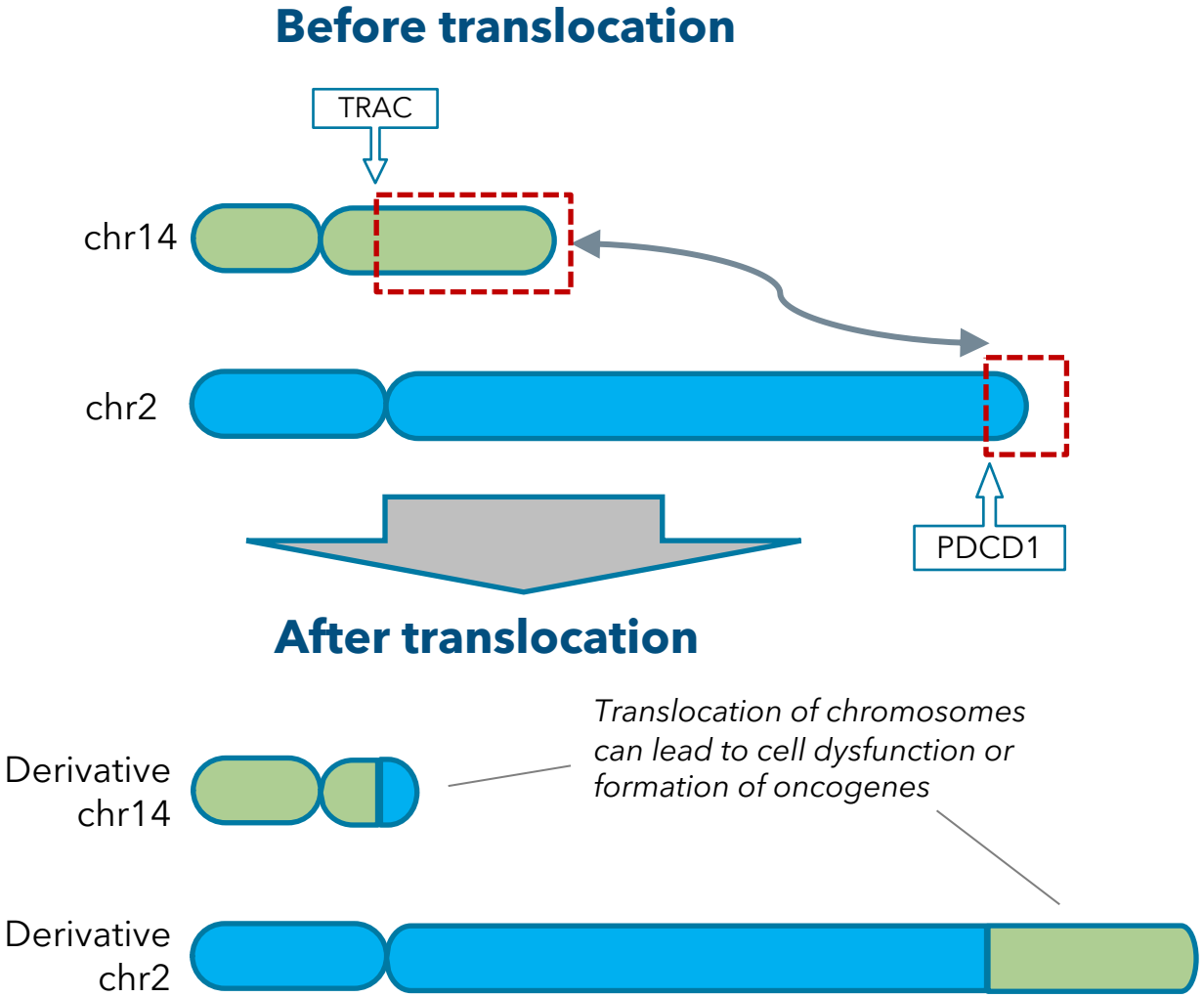
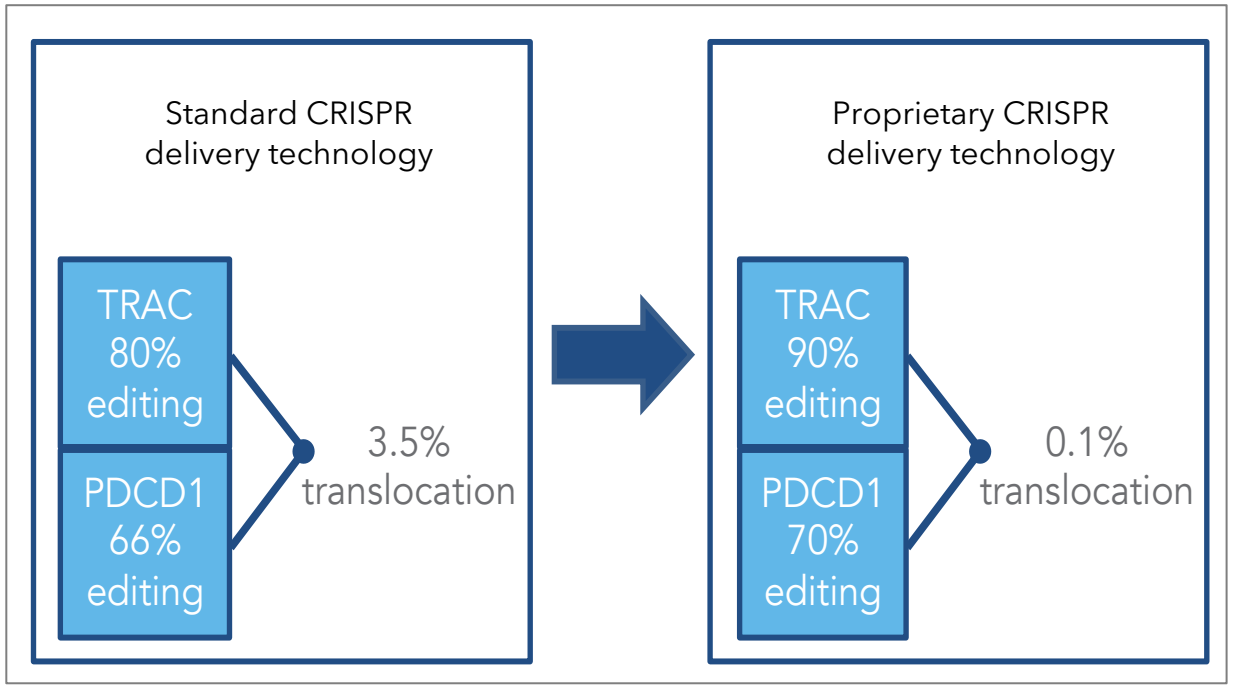
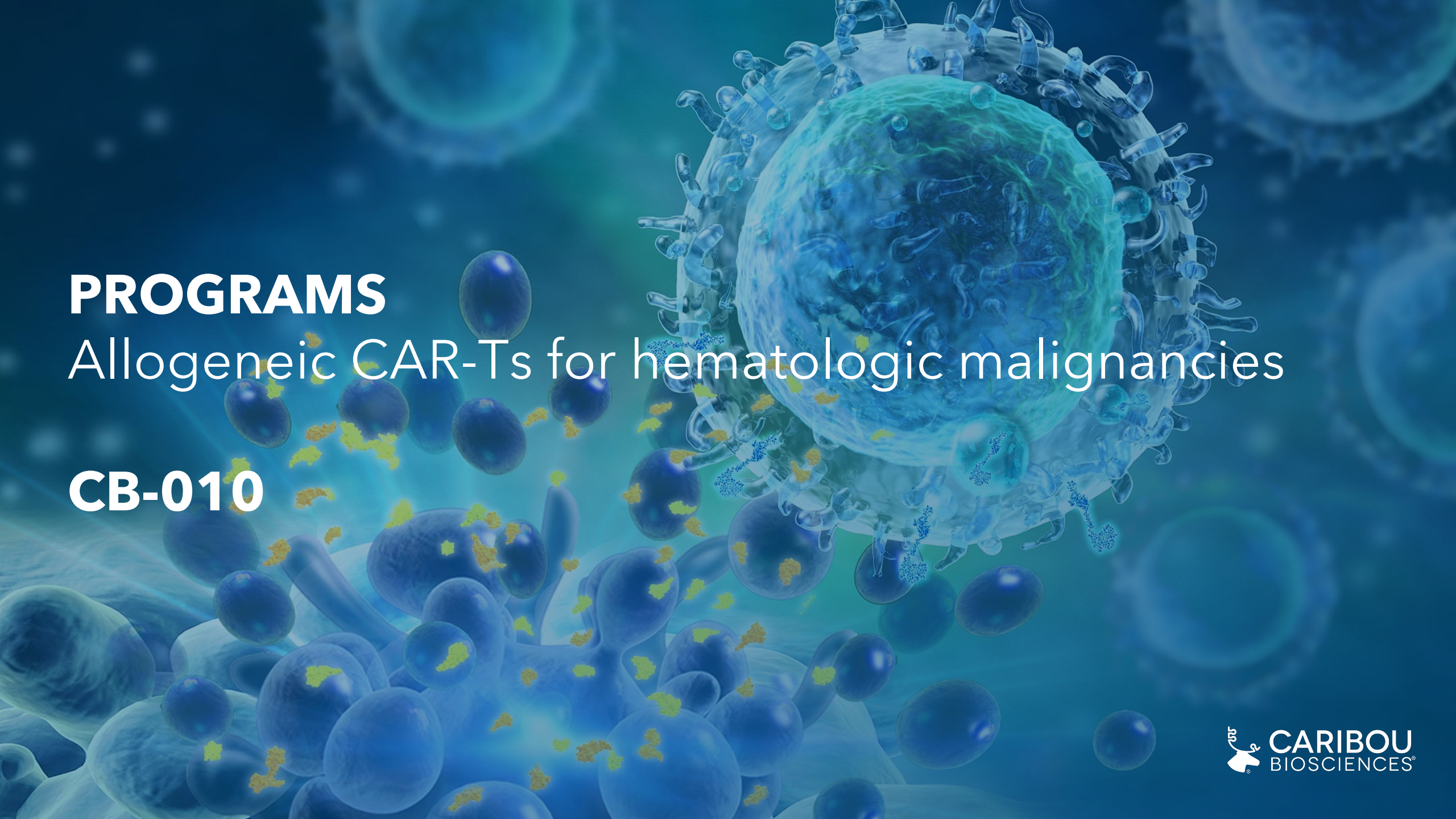
Multiplex editing: proprietary approach maintains genomic integrity with reduced translocations







PROGRAMS

Allogeneic CAR-Ts for hematologic malignancies

CB-010

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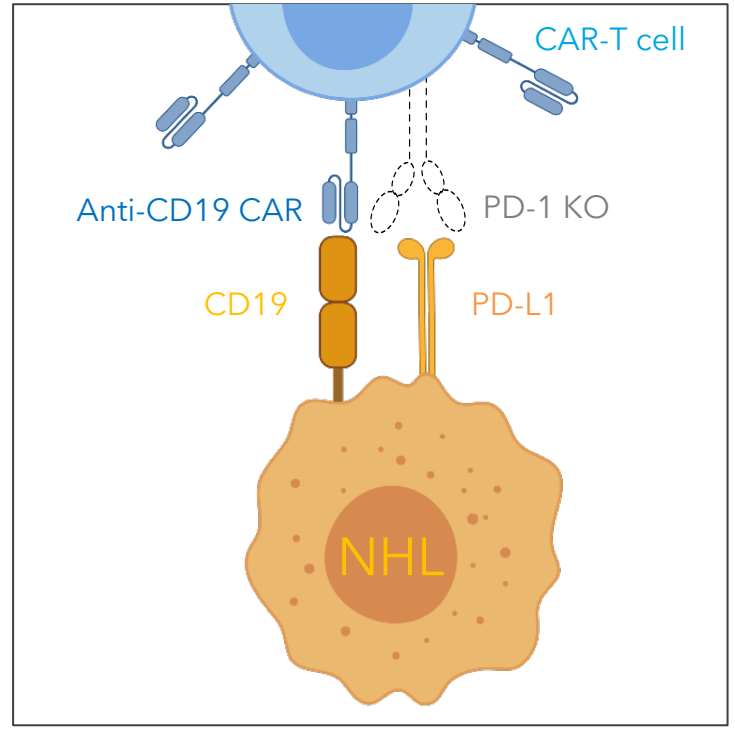
CB-010: anti-CD19 allogeneic CAR-T cell therapy

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

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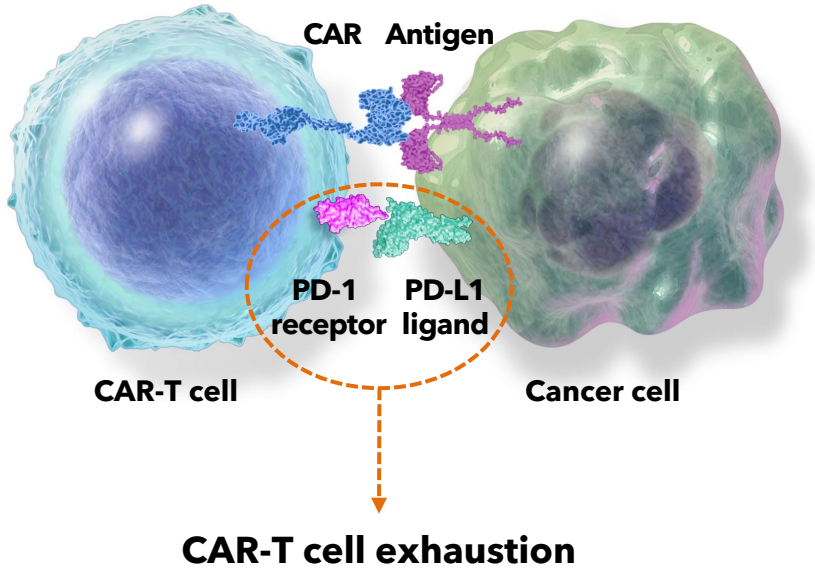
PD-1 KO designed to reduce CAR-T cell exhaustion

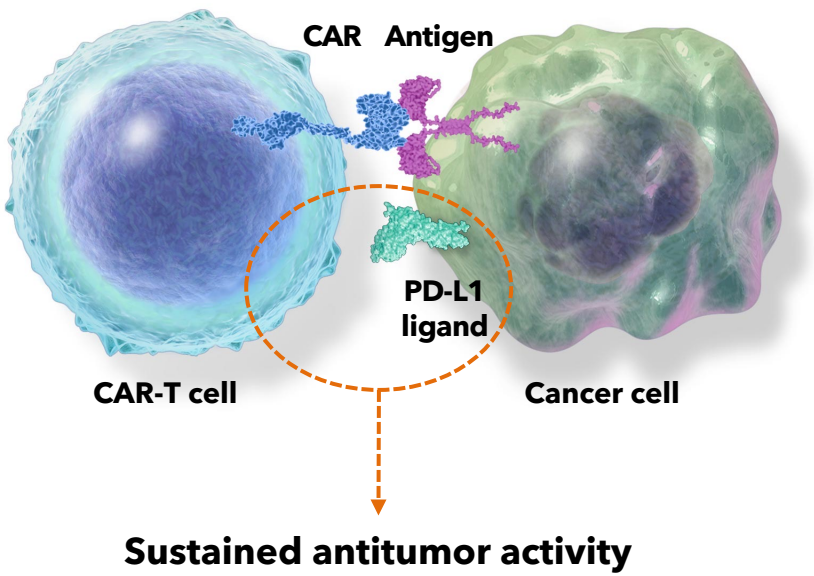
Conventional allogeneic CAR-T cell therapy

The PD-L1 ligand on cancer cells binds to the PD-1 receptor on a conventional allo CAR-T cell, limiting the CAR-T cell's killing ability



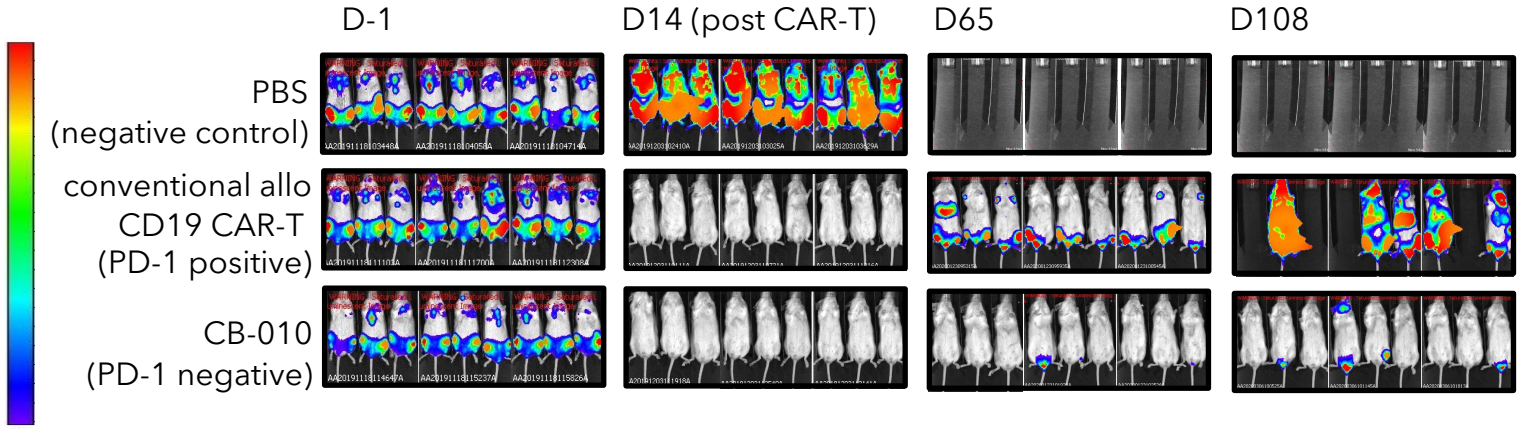
CB-010 CAR-T cell therapy

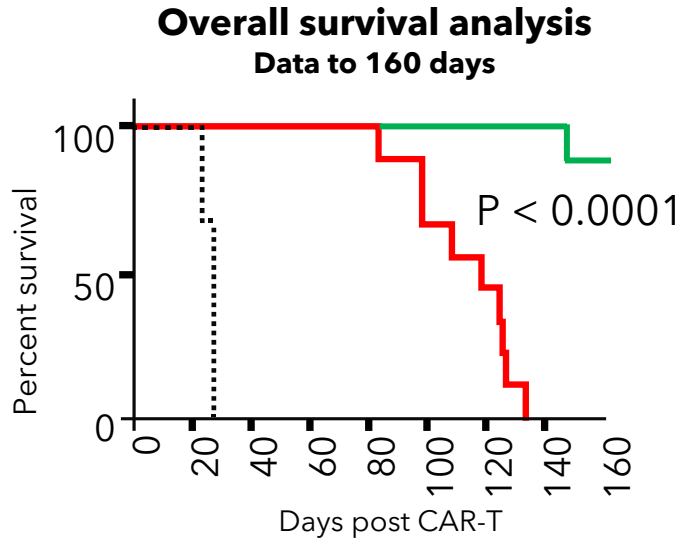
CB-010 cells lack PD-1 receptors on their surface and therefore are insensitive to PD-L1 interaction. CB-010 cells are designed to maintain high antitumor activity for a longer duration



CB-010 maintains persistent tumor eradication longer than conventional allo CAR-T cells

In preclinical studies, a single dose of CB-010 resulted in profound tumor regression of metastatic CD19⁺ tumor xenografts and led to a significantly more durable antitumor response
vs. conventional CD19-specific allo CAR-T cells (expressing PD-1)

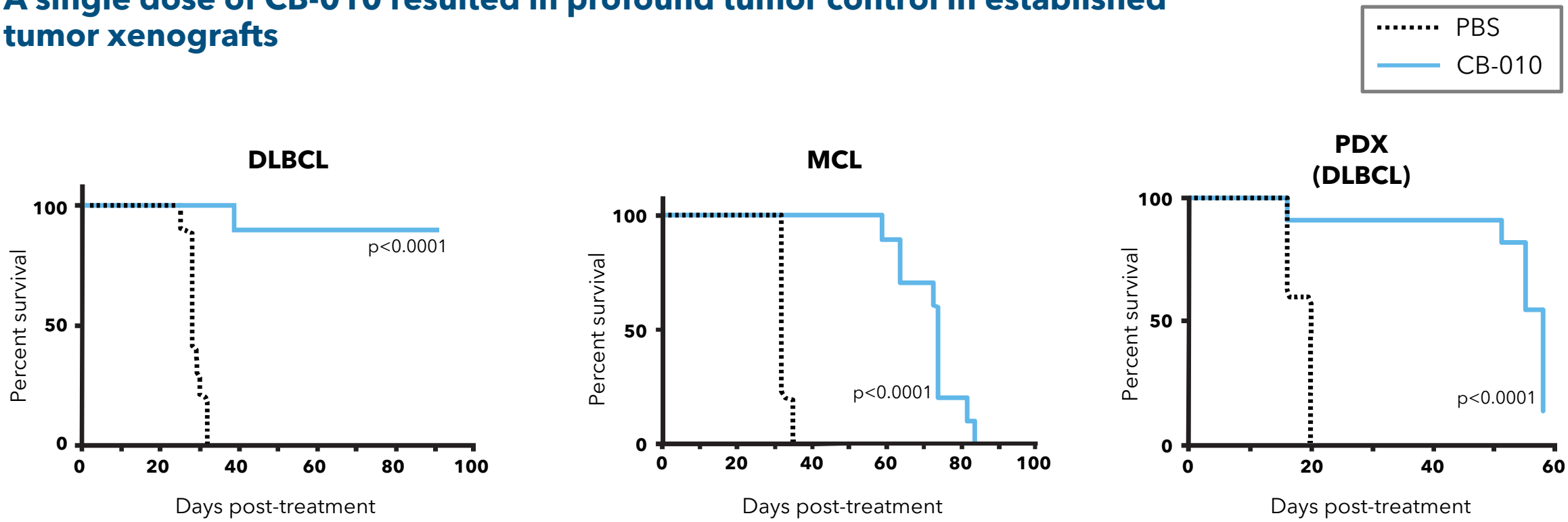




- NALM-6/PD-L1⁺ B-ALL tumors were established by IV engraftment for 23 days (Day -1)
- A single dose treatment was administered by IV on Day 24 (PBS or 10^7 cells where indicated)

CB-010 demonstrates statistically significant preclinical survival benefit across B-NHL indications

A single dose of CB-010 resulted in profound tumor control in established tumor xenografts



DLBCL: diffuse large B cell lymphoma
MCL: mantle cell lymphoma
PDX: patient-derived xenograft of DLBCL

CB-010 ANTLER Phase 1 open-label clinical trial

r/r B-NHL
(DLBCL, HGBL, tFL, PMBCL, FL, MZL, MCL)

B-NHL tumors are often PD-L1+

Adults who have failed 2 lines of chemo-immunotherapy
(will enroll up to 50 patients)
Exclusion: prior CD19 targeted therapy

Part A
3+3 dose escalation

Dose level 3

Dose level 2

Dose level 1

Primary objective:
- Safety and tolerability

Secondary objective:
- Preliminary efficacy

Part B
Expansion phase with RP2D in certain responding B-NHL subtypes

Primary objective:
- Efficacy in defined subtype population

Secondary objective:
- Safety, tolerability, additional efficacy endpoints

- Lymphodepletion (cy/flu combo[1]) involves a more intensive regimen, enabling improved engraftment and potentially enhanced efficacy
- Lymphodepletion regimen used in ANTLER was developed by NIH >10 years ago, previously demonstrated with TIL[2] and auto CAR-T cell therapies

Clinicaltrials.gov NCT#04637763

[1] Cyclophosphamide at 60 mg/kg/d for 2 days, then fludarabine at 25 mg/m²/d for 5 days

[2] Clin Cancer Res. 2011 July 1; 17(13): 4550–4557. doi:10.1158/1078-0432.CCR-11-0116.

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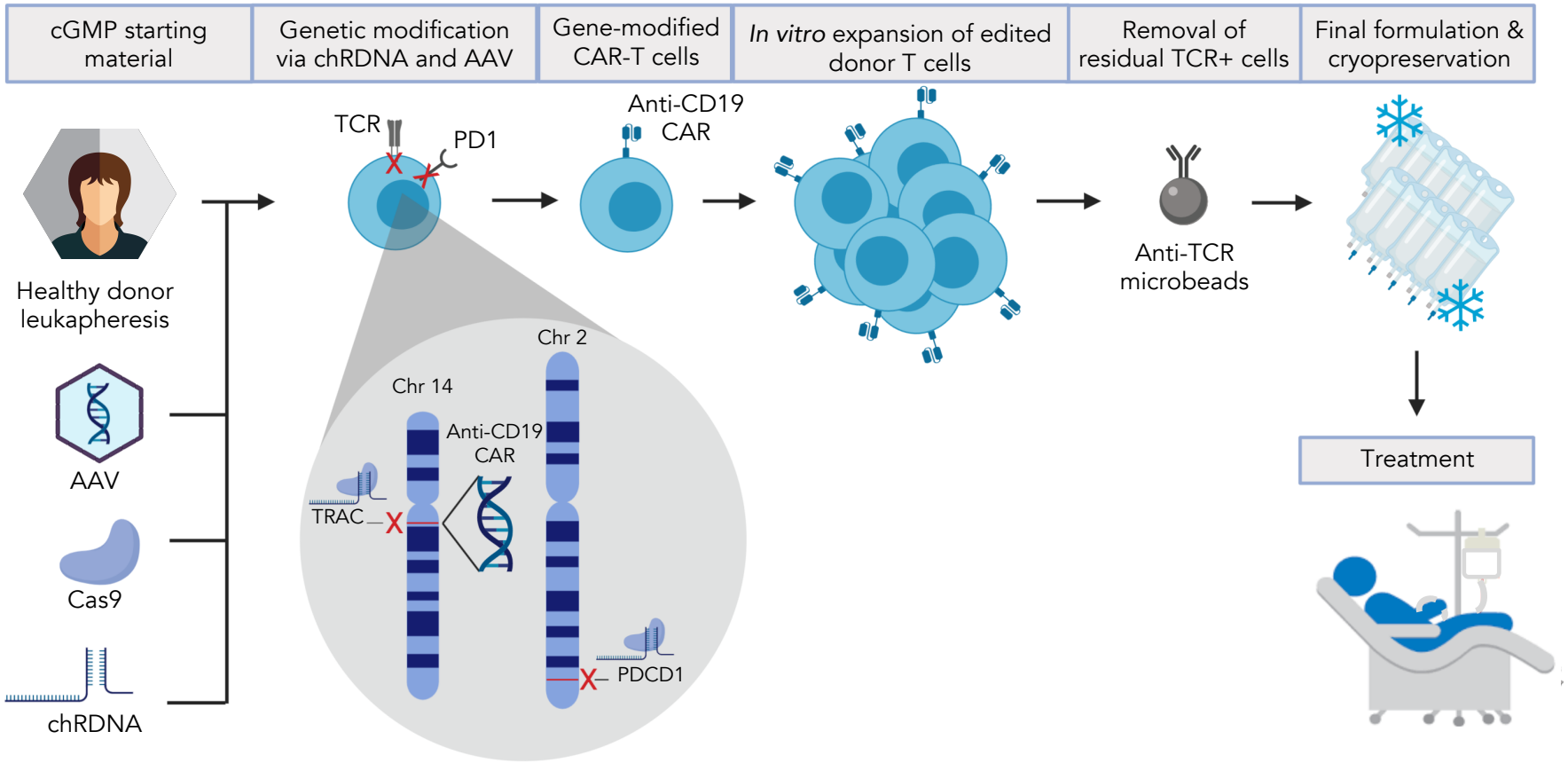
Allogeneic CAR-T cell manufacturing process overview for CB-010

Caribou's process development team created the manufacturing process and transferred it to a CMO to generate phase 1 cGMP clinical material



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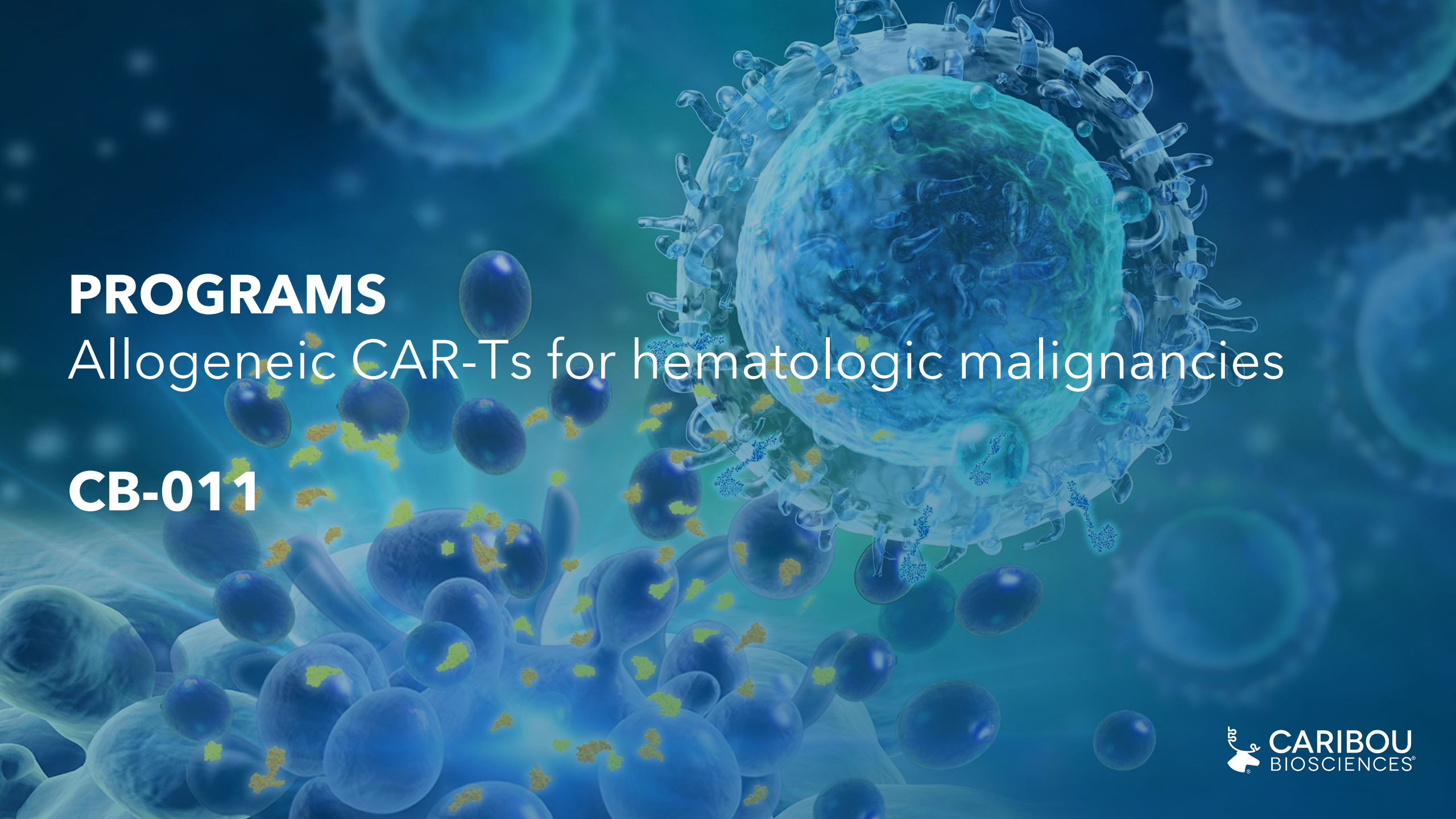
CB-010 summary: designed to diminish premature CAR-T cell exhaustion

- To our knowledge, CB-010 is the first clinical-stage allogeneic anti-CD19 CAR-T cell therapy with a PD-1 knockout
- The PD-1 knockout is designed to limit premature CAR-T cell exhaustion leading to:
  - Better tumor debulking preclinically
  - Potential for better therapeutic index (TI) through sustained antitumor activity
- Continuing to enroll patients in ANTLER phase 1 trial
- Plan to disclose initial clinical data from ANTLER in 2022



PROGRAMS

Allogeneic CAR-Ts for hematologic malignancies

CB-011

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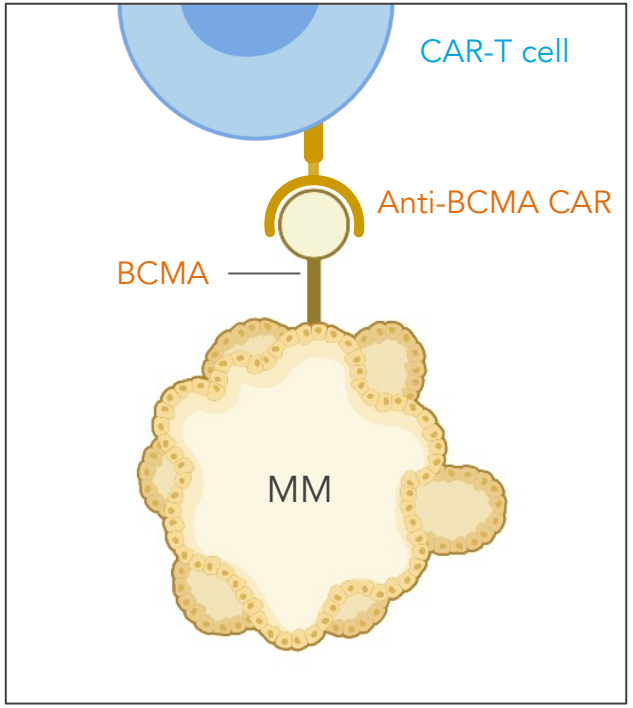
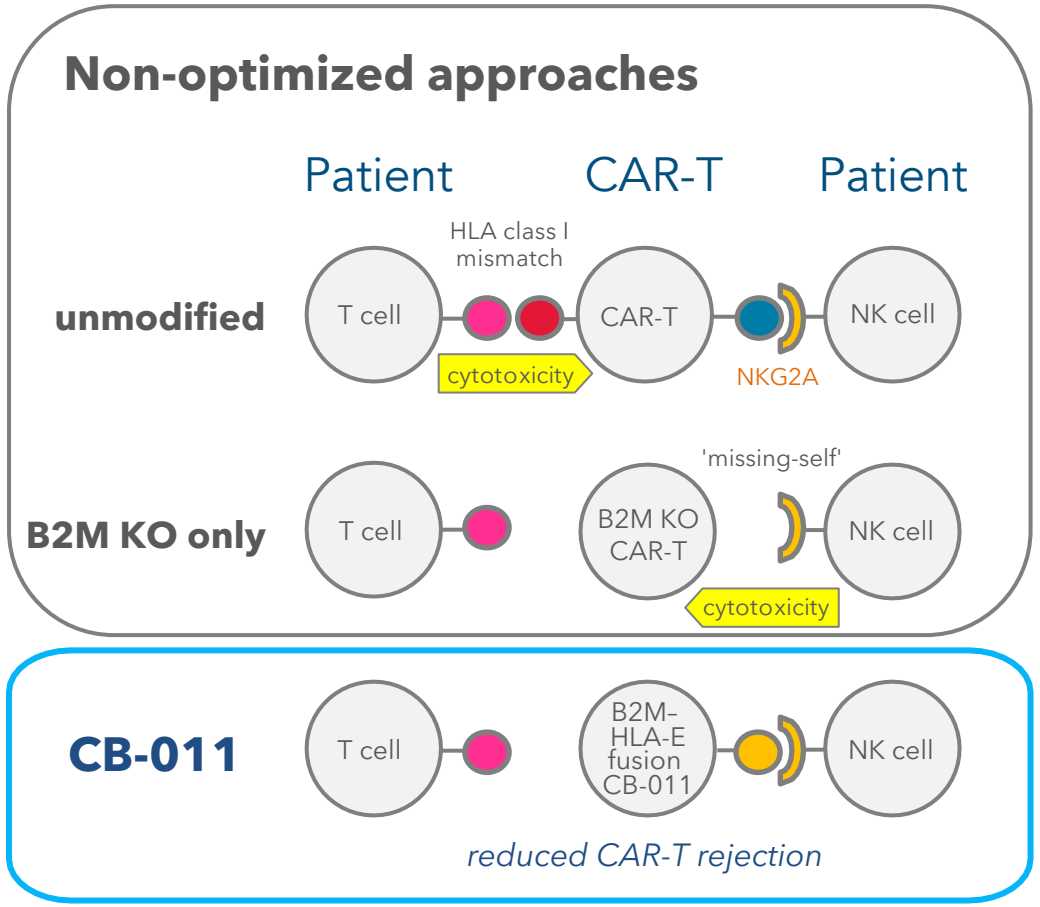
CB-011: anti-BCMA allogeneic CAR-T cell therapy

Key attributes	CB-011	Conventional allo anti-BCMA CAR-Ts
Immune cloaking strategy to prevent rapid immune rejection of the CAR-T • B2M KO + B2M–HLA-E–peptide fusion insertion	✓	X
Highly potent, proprietary, humanized anti-BCMA CAR	✓	Varies
Site-specific insertion of CAR into *TRAC* locus • Eliminates random integration and reduces risk of GvHD	✓	Varies
Cas12a chRDNA editing for enhanced genomic integrity • Reduced off-target editing	✓	X
Multiplex, site-specific gene insertions for enhanced product activity	✓	X



Program: CB-011
Tumor antigen: BCMA
Healthy donor leukapheresis-derived T cells
Indication: r/r multiple myeloma (MM)
Status: IND-enabling studies

CB-011: cloaking to prevent rapid immune-mediated rejection

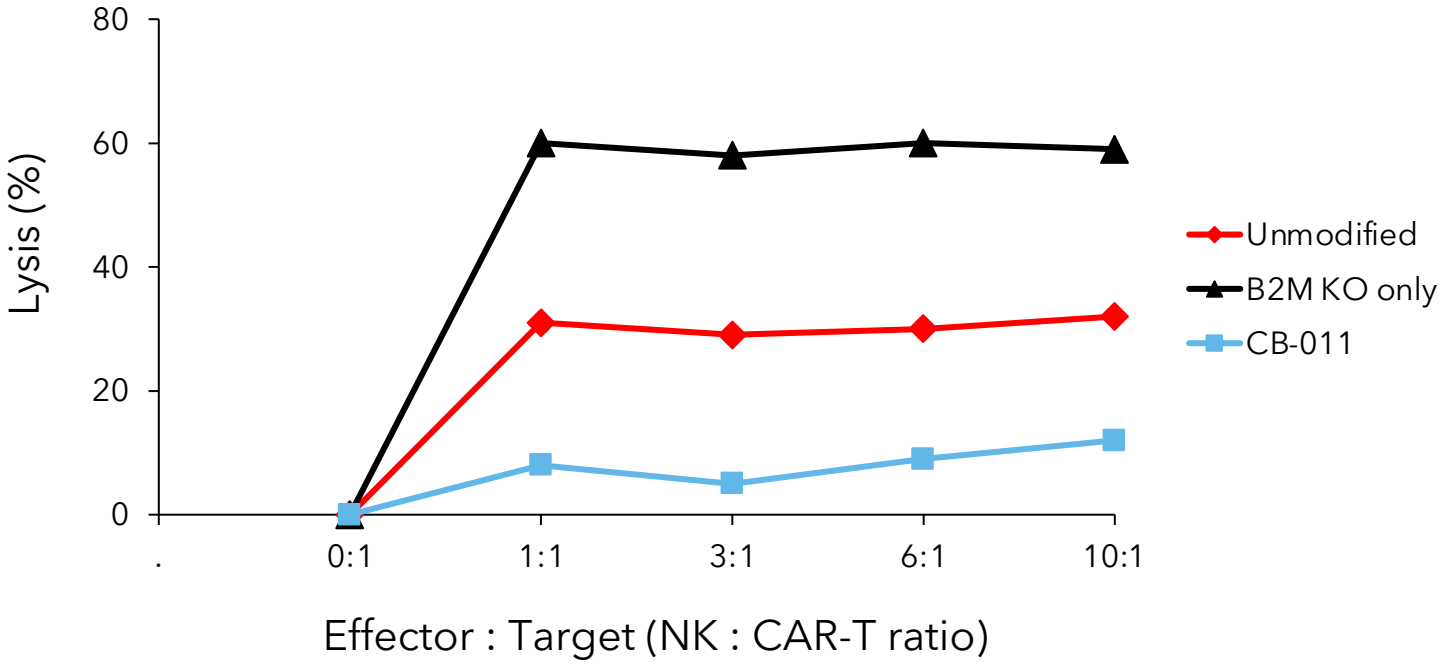


- B2M KO removes all endogenous HLA class I presentation to prevent T cell-mediated rejection
- B2M-HLA-E-peptide insertion prevents NK cell-mediated rejection
- The Cas12a chRDNA editing platform achieves sufficiently high insertion efficiencies to simultaneously insert B2M-HLA-E-peptide and CAR into different genomic locations

The B2M–HLA-E fusion protects CB-011 CAR-T cells *in vitro* from NK cell-mediated lysis

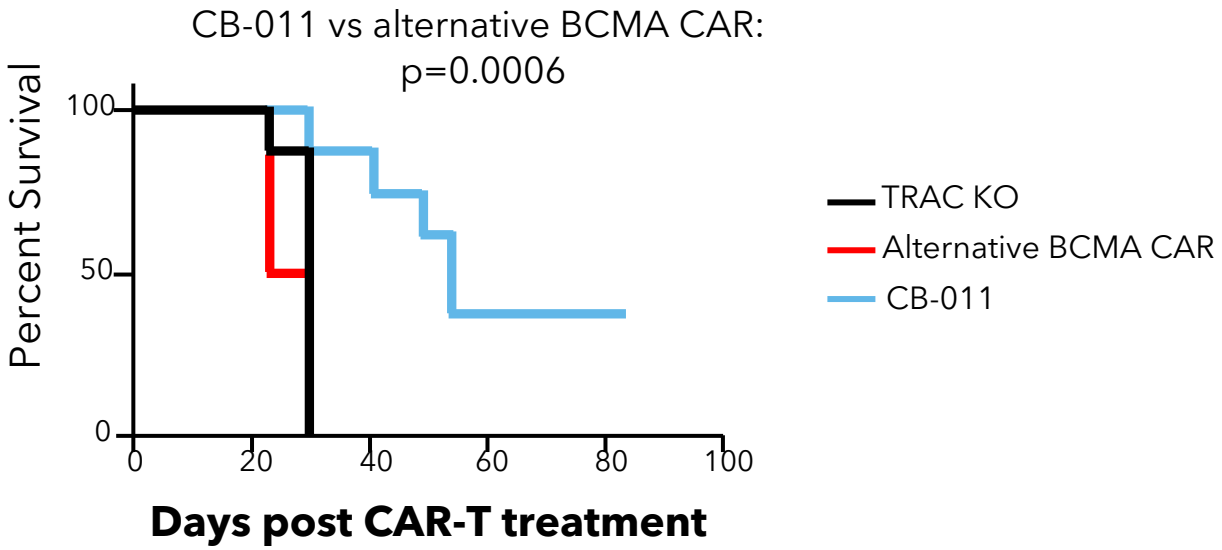
The B2M–HLA-E fusion enables CB-011 cells to resist killing by NK cells

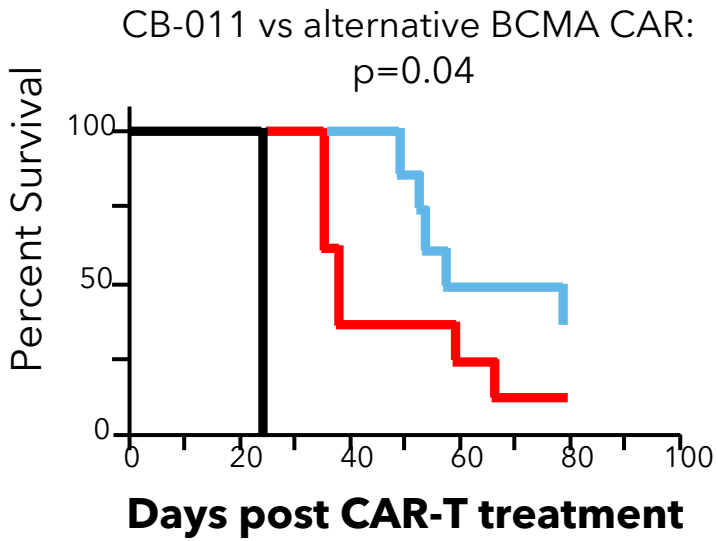
in vitro cytotoxicity measured 24 hours after CAR-T cell co-incubation with NK-92 cells



CB-011: proprietary, potent CAR enhances long-term survival in preclinical studies

CB-011 led to statistically significant and longer survival of tumor-bearing mice
relative to an alternative anti-BCMA CAR-T cell therapy after a single dose





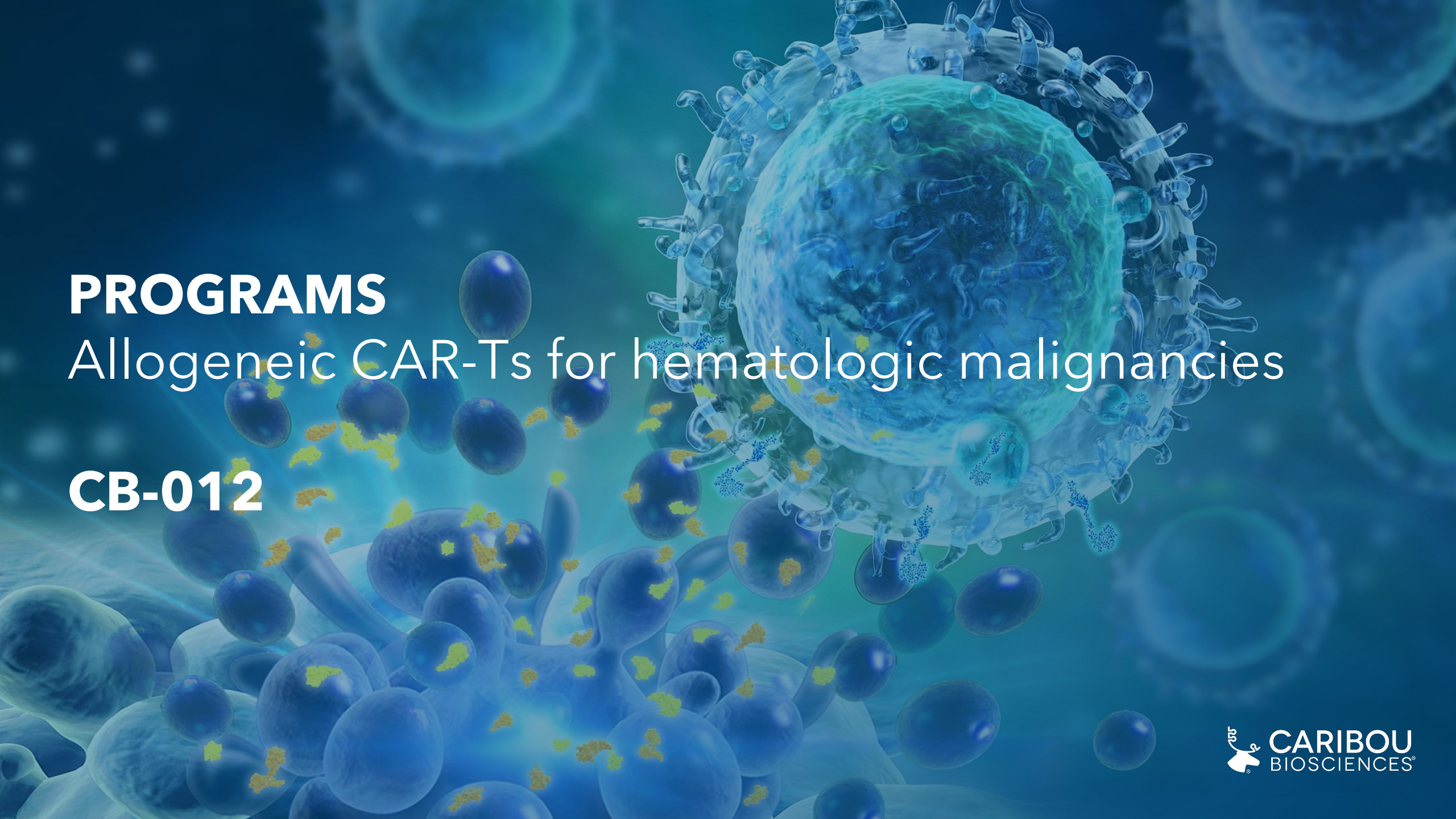
- Established subcutaneous multiple myeloma tumor xenograft
- Single dose CAR-T cell treatment

- Established orthotopic BCMA^{+} tumor xenograft
- Single dose CAR-T cell treatment

CB-011 summary: immune-cloaked to enhance persistence

- To our knowledge, CB-011 is the first allogeneic CAR-T cell therapy for MM immune cloaked to prevent both T- and NK-mediated rejection
  - The immune cloaking strategy is intended to drive CAR-T cell persistence for more durable antitumor activity
- CB-011 uses a patented[1], potent, humanized anti-BCMA CAR
  - Robust preclinical data in MM tumor xenografts
- IND filing planned for 2022

1. Three U.S. patents granted to date



PROGRAMS

Allogeneic CAR-Ts for hematologic malignancies

CB-012

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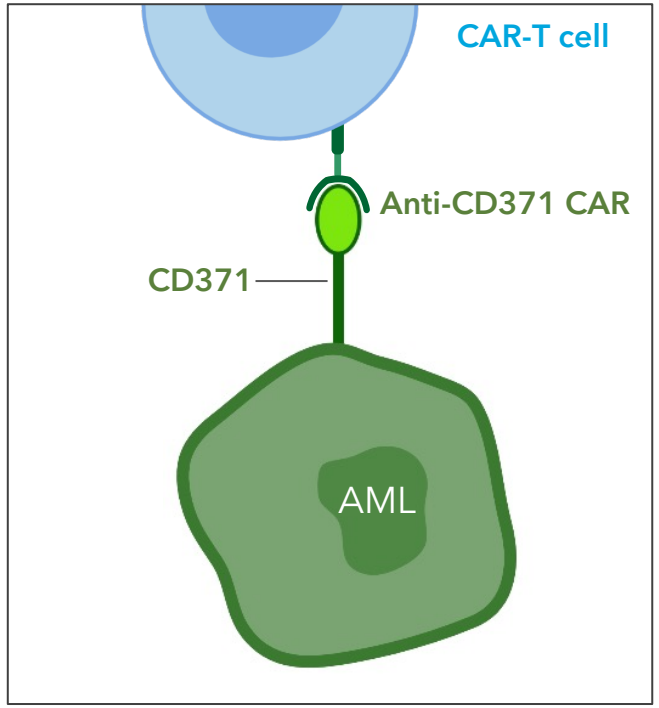
CB-012: anti-CD371 allogeneic CAR-T cell therapy for AML

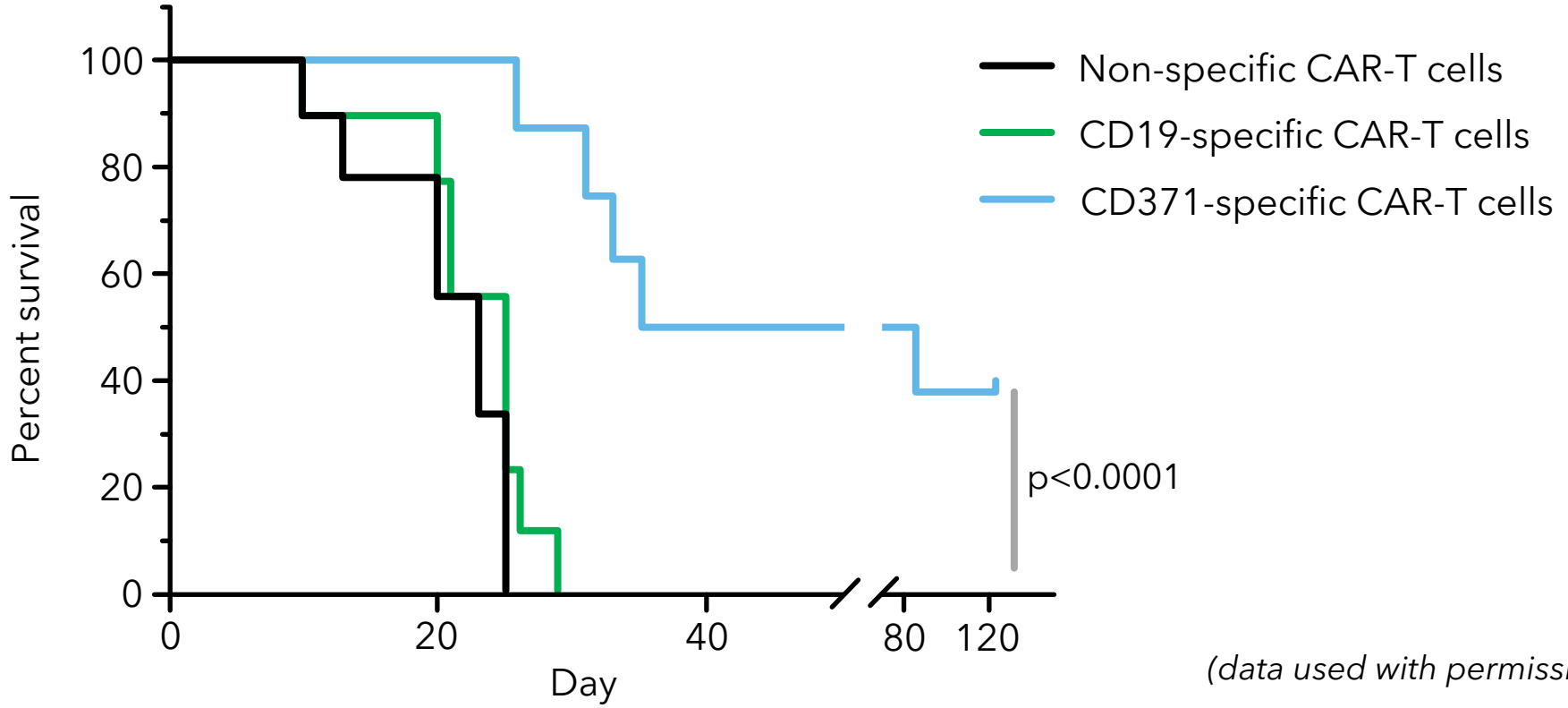
Key attributes	CB-012	Other allo CAR-Ts for AML
CD371 target	✓	X
• Target not expressed on HSCs	✓	Varies
Potent, fully human anti-CD371 CAR	✓	X
Site-specific insertion of CAR into *TRAC* locus • Eliminates random integration and reduces risk of GvHD	✓	Varies
Armoring for enhanced persistence, efficacy	✓	X
Cas12a chRDNA editing for enhanced genomic integrity	✓	X



Program: CB-012
Tumor antigen: CD371
Healthy donor leukapheresis-derived T cells
Indication: r/r acute myeloid leukemia (AML)
Status: discovery

CD371-specific CAR-T cells confer long-term survival in a xenograft model of AML

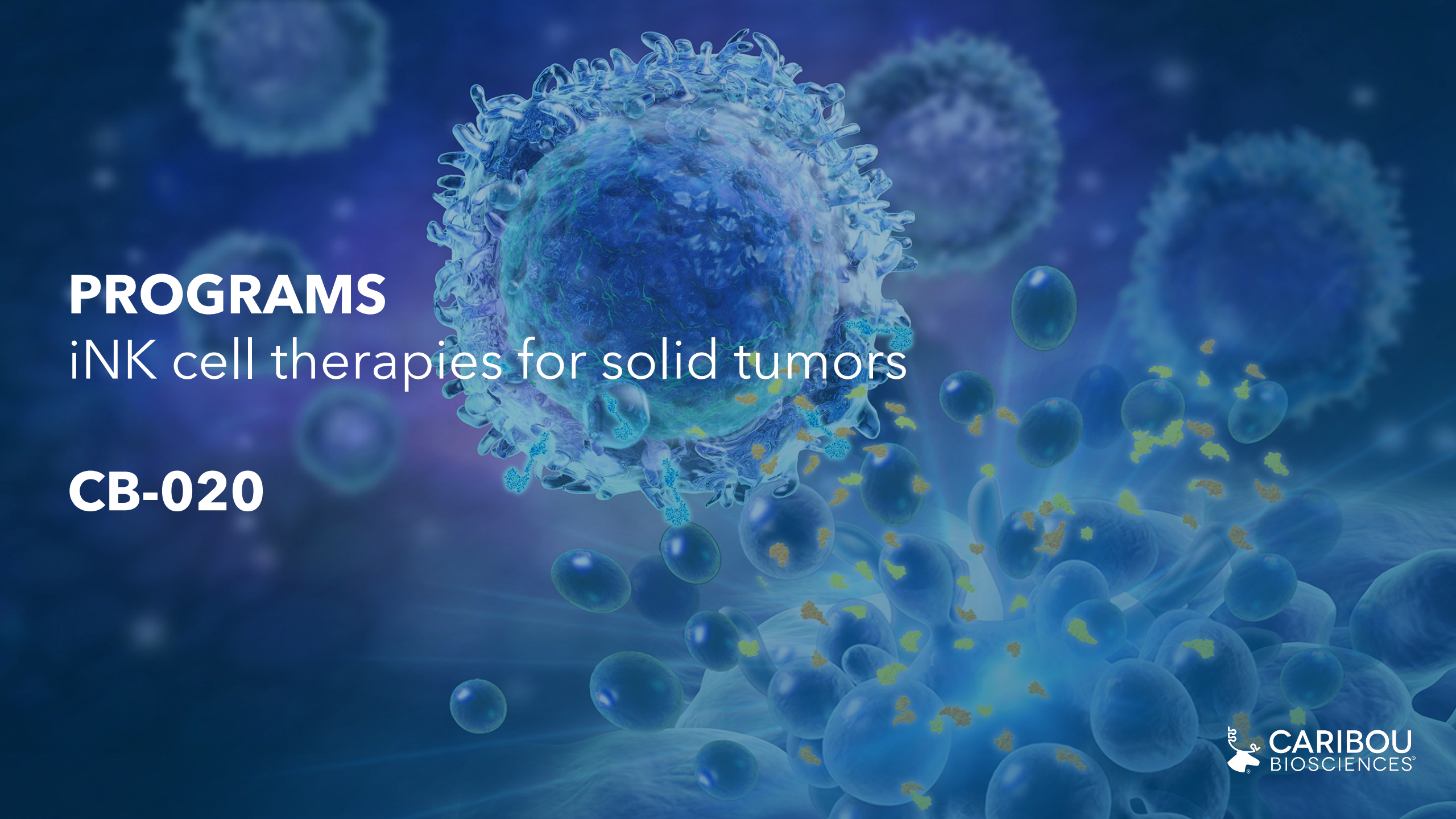
Researchers at MSKCC conducted a study evaluating one of the fully human CD371-specific scFvs exclusively licensed to Caribou for allogeneic cell therapies



(data used with permission from MSKCC)

CB-012 summary: armored allogeneic CAR-T for AML

- CB-012 is an allogeneic anti-CD371 CAR-T cell therapy for the treatment of r/r AML
- Caribou is using Cas12a chRDNA technology to armor CB-012 and improve the persistence of antitumor activity
- CD371 is a compelling target for AML
  - CD371 is expressed on tumor cells and leukemic stem cells, but not expressed on normal HSCs
  - Caribou exclusively licensed fully human anti-CD371 scFvs from MSKCC
- Other AML targets are expressed on normal HSCs as well as tumor cells
  - CAR-T cell activity against normal HSCs may require HSC transplant following CAR-T cell treatment
- IND filing planned for 2023



PROGRAMS

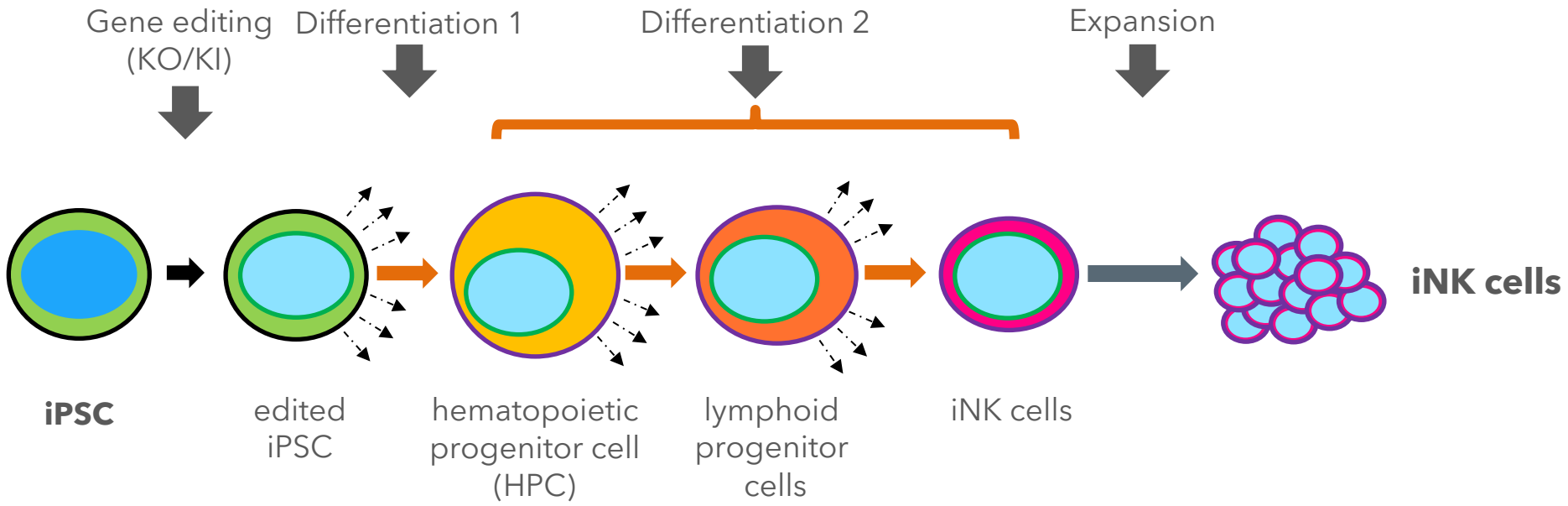
iNK cell therapies for solid tumors

CB-020

CARIBOU BIOSCIENCES®

CB-020 is an iPSC-derived CAR-NK cell therapy for solid tumor targeting

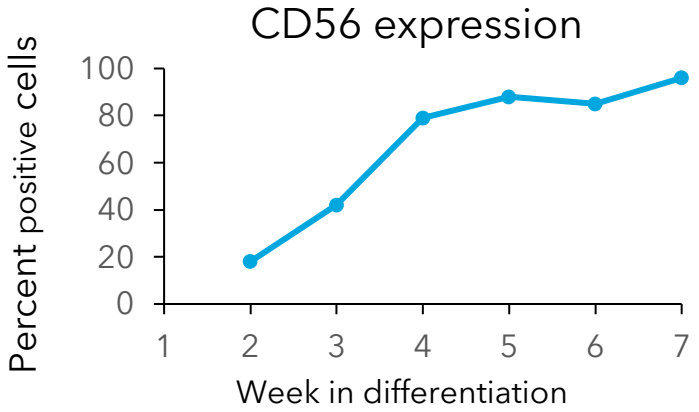
- CAR-T cells generally have not demonstrated broad, robust antitumor activity in solid tumors
- Natural killer (NK) cells are allogeneic and inherently target solid tumors and metastases
- Edited iNKs as cell therapies derived from edited iPSCs are a compelling platform for solid tumor-targeting cell therapy development
- Caribou has developed robust differentiation and expansion protocols to derive iNKs from iPSCs

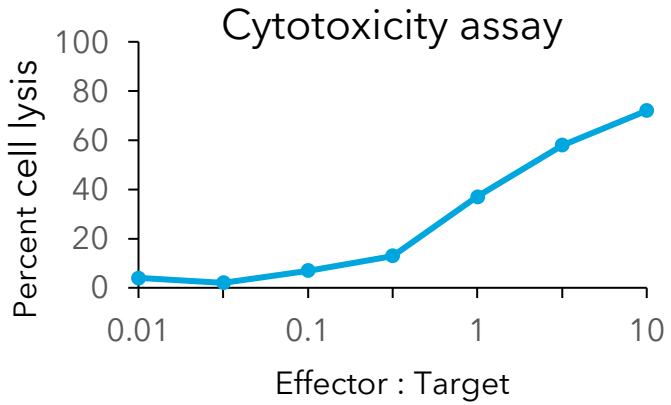


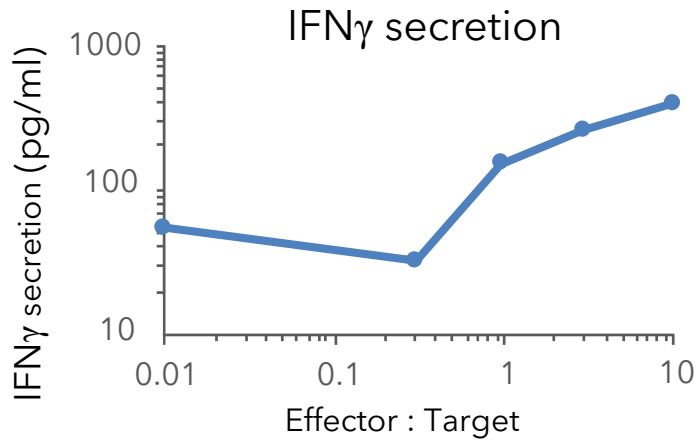
iNK cells demonstrate expected polyfunctionality similar to primary NK cells

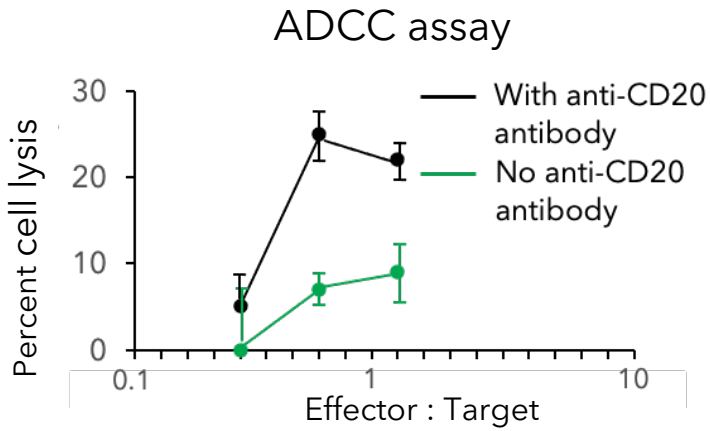
iPSCs were differentiated into CD56⁺ iNKs exhibiting cytotoxic activity and interferon gamma (IFNγ) secretion

iNKs also kill target cells by antibody-dependent cell cytotoxicity (ADCC)







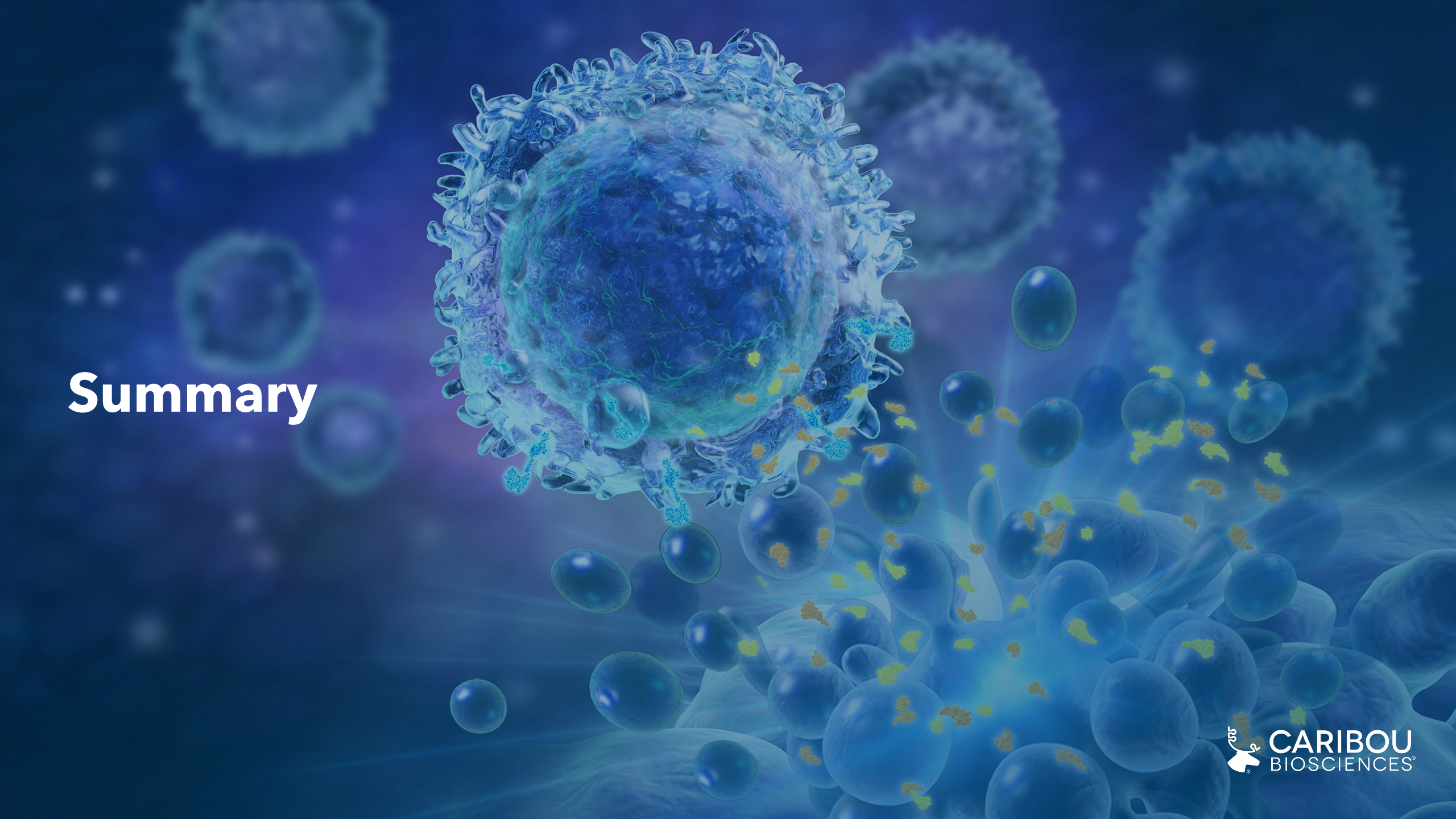


CARIBOU BIOSCIENCES®

Caribou's iNK platform holds the potential for future cell therapies targeting solid tumors

- NK cells natively demonstrate potent antitumor activity against primary solid tumors and metastases
- Caribou's multiplex edited iPSC-to-iNK platform is designed to address fundamental challenges with targeting solid tumors and metastatic sites
  - Trafficking, tumor infiltration, surviving the immunosuppressive tumor microenvironment, overcoming heterogeneity, persistence
- Caribou has developed a robust and reproducible platform for differentiating iPSCs into iNK cells
  - Generates an iNK cell population 100% edited for multiple genomic modifications
- Caribou has multiple armoring strategies to distinguish CB-020 using its proprietary genome-editing technologies

Summary



CARIBOU BIOSCIENCES®

Focused on execution – upcoming milestones

2021 and YTD accomplishments

- **Continuing to enroll patients in ANTLER phase 1 clinical trial**
- **Collaboration agreement with AbbVie executed**
- **Completed IPO in Q321 ($321M net proceeds)**
- **Added CFO, CBO, and CMO**
- **Strengthened Board of Directors with the addition of 5 new directors**
- **Expanded SAB**

Future anticipated milestones

- **CB-010**
  Disclosure of initial phase 1 data expected 2022
- **CB-011**
  IND filing 2022
- **CB-012**
  IND filing 2023
- **CB-020**
  Target selection 2022

Thank you

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Experienced management team

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Director

Steve Kanner, PhD
Chief Scientific Officer

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Chief Financial Officer

Syed Rizvi, MD
Chief Medical Officer

Barbara McClung, JD
Chief Legal Officer
and Corporate
Secretary

Ruhi Khan
Chief Business Officer