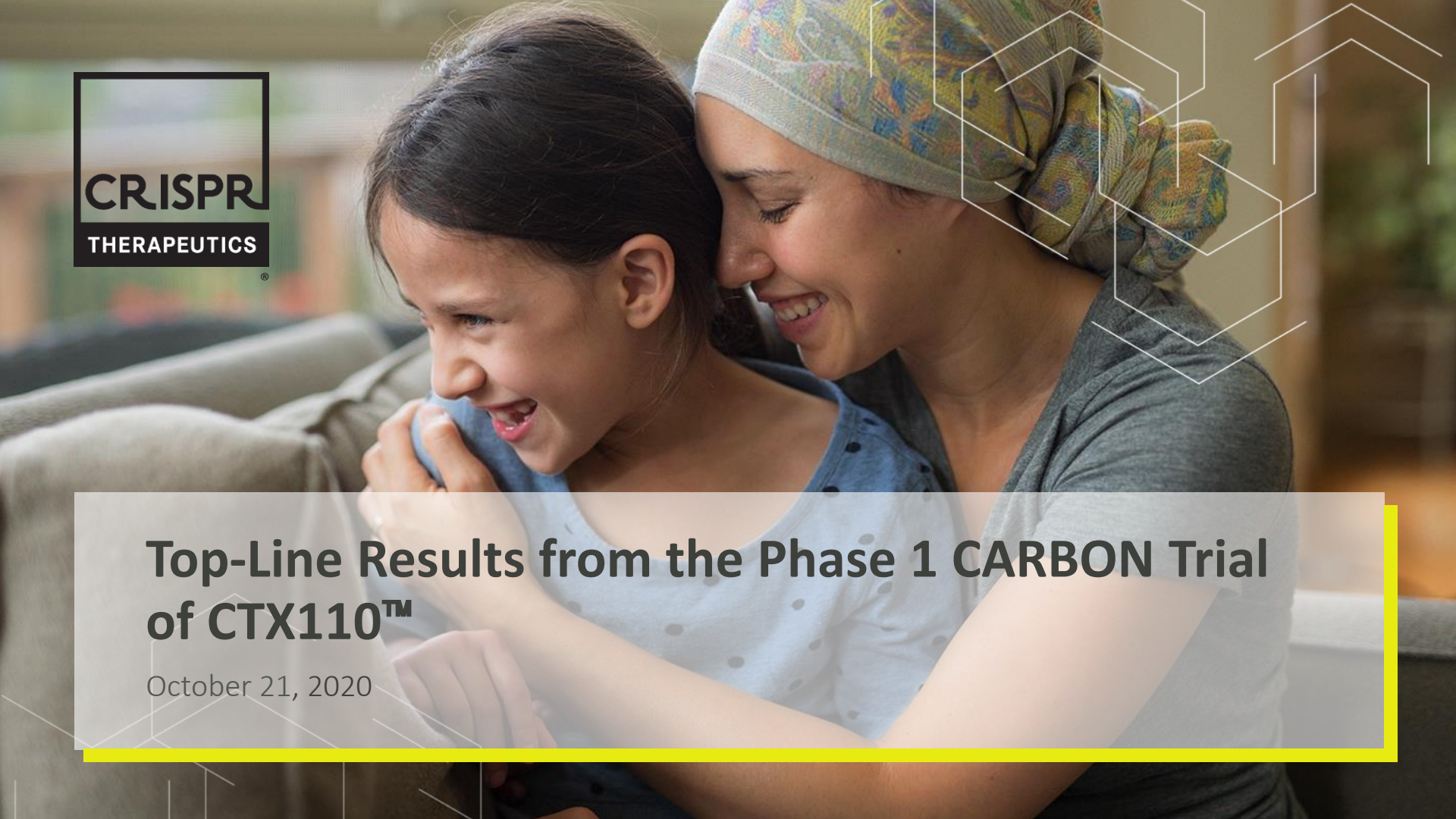

Top-Line Results from the Phase 1 CARBON Trial of CTX110™

October 21, 2020

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The presentation and other related materials may contain a number of "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including statements regarding CRISPR Therapeutics' expectations about any or all of the following: (i) the safety, efficacy and clinical progress of our various clinical programs; (ii) the status of clinical trials (including, without limitation, the expected timing of data releases, announcement of additional programs and activities at clinical trial sites) and expectations regarding the data that is being presented; (iii) the data that will be generated by ongoing and planned clinical trials, and the ability to use that data for the design and initiation of further clinical trials; and (iv) the therapeutic value, development, and commercial potential of CRISPR/Cas9 gene editing technologies and therapies, including as compared to other therapies. Without limiting the foregoing, the words "believes," "anticipates," "plans," "expects" and similar expressions are intended to identify forward-looking statements. You are cautioned that forward-looking statements are inherently uncertain. Although CRISPR Therapeutics believes that such statements are based on reasonable assumptions within the bounds of its knowledge of its business and operations, forward-looking statements are neither promises nor guarantees and they are necessarily subject to a high degree of uncertainty and risk. Actual performance and results may differ materially from those projected or suggested in the forward-looking statements due to various risks and uncertainties. These risks and uncertainties include, among others: the potential for initial and preliminary data from any clinical trial and initial data from a limited number of patients not to be indicative of final trial results; the potential that clinical trial results may not be favorable; potential impacts due to the coronavirus pandemic, such as the timing and progress of clinical trials; that future competitive or other market factors may adversely affect the commercial potential for CRISPR Therapeutics' product candidates; uncertainties regarding the intellectual property protection for CRISPR Therapeutics' technology and intellectual property belonging to third parties, and the outcome of proceedings (such as an interference, an opposition or a similar proceeding) involving all or any portion of such intellectual property; and those risks and uncertainties described under the heading "Risk Factors" in CRISPR Therapeutics' most recent annual report on Form 10-K, quarterly report on Form 10-Q and in any other subsequent filings made by CRISPR Therapeutics with the U.S. Securities and Exchange Commission, which are available on the SEC's website at www.sec.gov. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date they are made. CRISPR Therapeutics disclaims any obligation or undertaking to update or revise any forward-looking statements contained in this presentation, other than to the extent required by law.

Presenters on Today's Call

Samarth Kulkarni, PhD

Chief Executive Officer
CRISPR Therapeutics

Ewelina Morawa, MD

Vice President, Clinical Development
CRISPR Therapeutics

Joseph McGuirk, DO

Professor of Medicine and Division Director of Hematologic Malignancies and Cellular Therapeutics
University of Kansas Medical Center

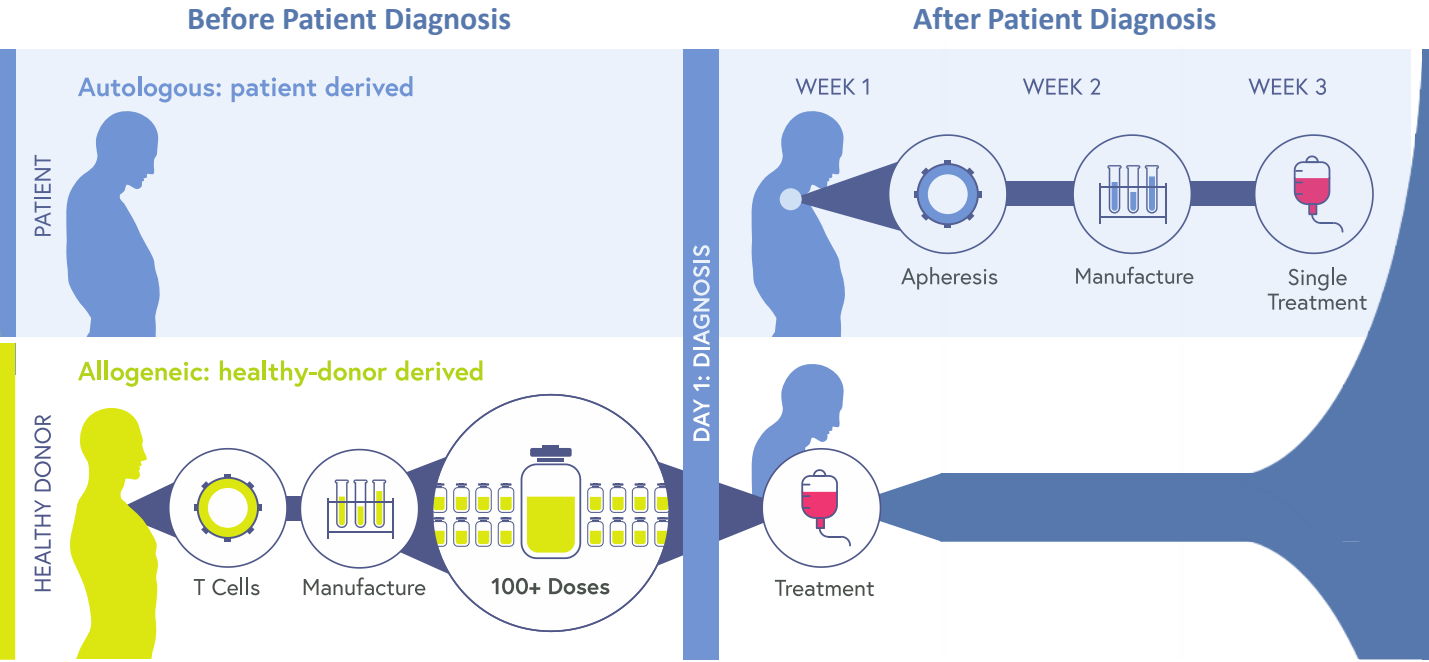
Tony Ho, MD

Executive Vice President, Head of Research & Development
CRISPR Therapeutics

We Have Made Tremendous Progress Over the Past 5 Years

- **Built the leading CRISPR company:** 4 programs in the clinic; >300 employees; >$1B cash balance
- **Demonstrated, for the first time, the power of CRISPR gene editing in rare diseases:** initial data with CTX001™ supportive of a potential functional cure for sickle cell disease and beta thalassemia
- **Advanced three gene-edited allogeneic CAR-T programs into the clinic** across four trials
- **In parallel, expanded into regenerative medicine and progressed our *in vivo* efforts**
- **Created a sustainable innovation engine with pre-eminent capabilities**
- **And today, we show the promise and potential of CRISPR-edited cell therapies in the fight against cancer**

Allogeneic CAR-T Therapy Has Transformative Potential



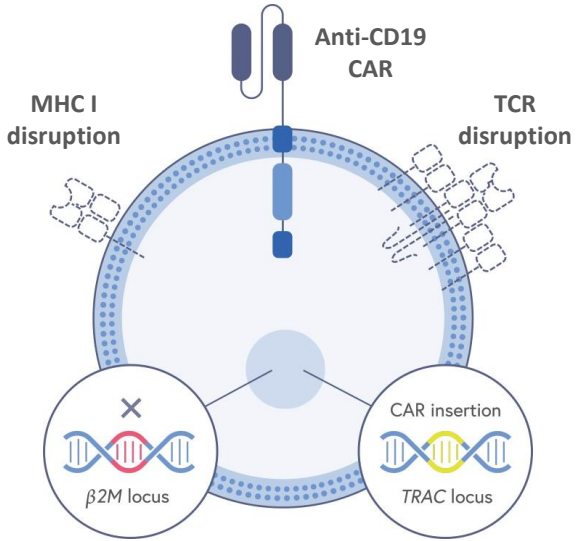
- **Off-the-shelf:** Immediate treatment without risk of manufacturing failure, saving patients valuable time in which their disease could progress
- **Flexible dosing** (e.g., re-dosing)
- **A more consistent product**
- **Scalable manufacturing and simpler logistics**
- **Broader accessibility**

*Specificity, efficiency, and versatility of **CRISPR gene editing** facilitates consistent, multiplex editing to produce allogeneic cell therapies and enhance immune cell performance*

CTX110: Differentiated CRISPR-Edited Allogeneic CAR-T Design

Multiplex CRISPR gene editing in one step designed to:

- **Improve persistence in the allo setting** via β2M knock-out to eliminate MHC I expression
- **Avoid need** for more toxic lymphodepletion regimens



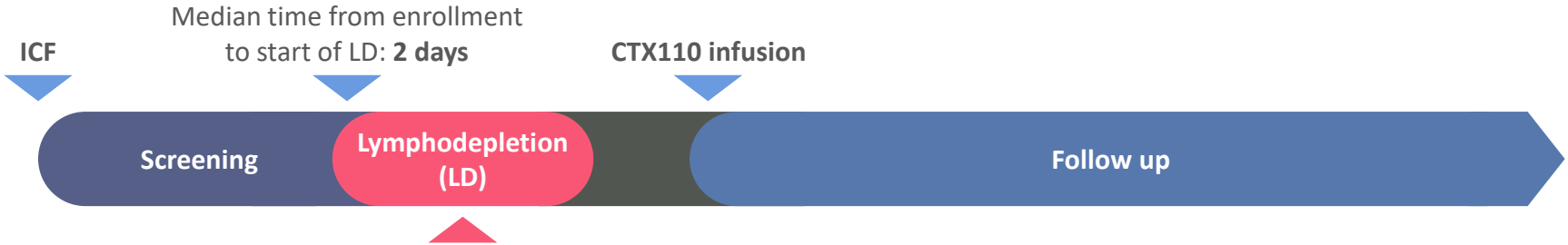
- **Prevent GvHD** via TCR disruption
- **Improve consistency and safety by precise insertion** of CAR construct into *TRAC* locus without using lentivirus or retrovirus

*CTX120™ and CTX130™ utilize the **same CRISPR-edited allogeneic T cell design**, but with different CAR targets, as well as additional editing in the case of CTX130*

CARBON: Trial Design

CARBON: Single-arm study evaluating the safety and efficacy of CTX110

Allogeneic CAR-T enables simplified trial design: short screening timeframe, no apheresis, no bridging chemotherapy, and on-site availability of CAR-T cell product



NCT04035434

Key eligibility criteria

- Age ≥18 years
- Relapsed/refractory non-Hodgkin lymphoma, as evidenced by 2+ lines of prior therapy
- ECOG performance status 0 or 1
- Adequate renal, liver, cardiac, and pulmonary organ function
- No prior allogeneic SCT or treatment with CAR-T therapy

Primary endpoints

- Incidence of adverse events, defined as DLTs
- ORR

Key secondary endpoints

- DoR, PFS, and OS

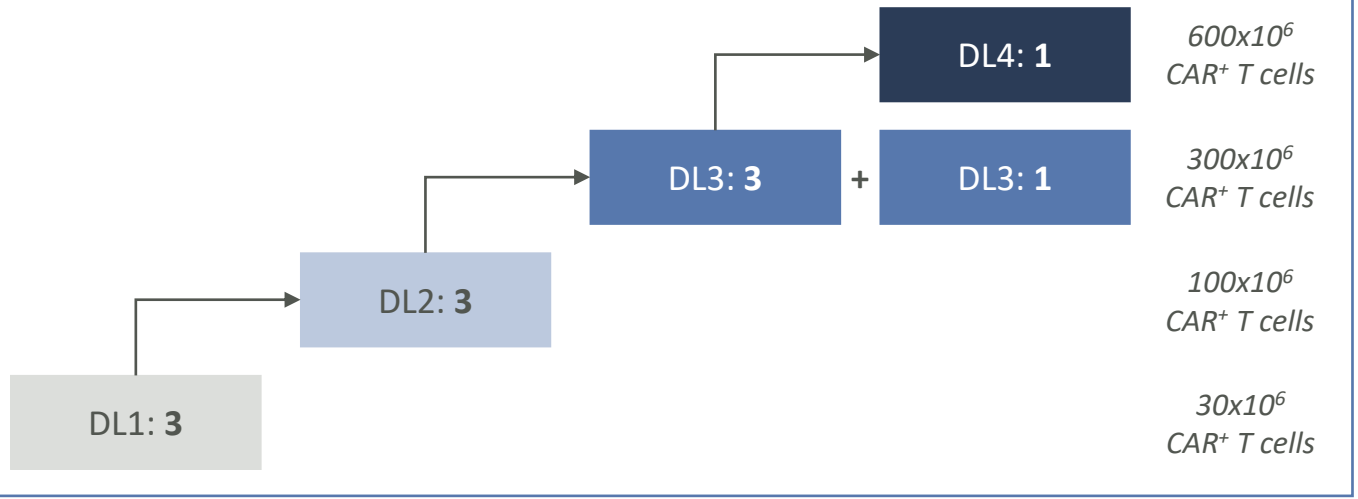
CARBON: Patient Flow

As of the data cutoff date:

Enrolled: **12** patients

Treated: **12** patients

At least 28 days of follow-up (included in data cut): **11** patients



- At each completed dose level, **two lots of CTX110 manufactured from different healthy donors** were used
- Given antitumor activity observed, **additional patients enrolled at DL3 and DL4 added**

Data as of September 28, 2020

CARBON: Baseline Patient Characteristics

N (%) (unless otherwise noted)

Cell dose (CAR+ T cells)	DL1 30x10^6 *N=3*	DL2 100x10^6 *N=3*	DL3 300x10^6 *N=4*	DL4 600x10^6 *N=1*
Median age, years (range)	52 (50-61)	64 (58-74)	64.5 (62-74)	72
Male	2 (66.7)	2 (66.7)	1 (25)	1 (100)
Lymphoma subtypes				
Diffuse large B-cell lymphoma (DLBCL)[1]	3 (100)	3 (100)	4 (100)	1 (100)
Follicular lymphoma	0	0	0	0
Current disease stage (per Lugano 2014)[2]				
Stage III	1 (33.3)	1 (33.3)	2 (50)	0
Stage IV	2 (66.7)	2 (66.7)	1 (25)	1 (100)
Prior treatments				
Median number (range)	2.0 (2-8)	3.0 (2-3)	2.0 (2-4)	5
Hematopoietic stem cell transplant	0	0	3 (75)	1 (100)
Refractory to last therapy	3 (100)	3 (100)	0	0

(1) Including high grade lymphoma (e.g., triple hit), transformed follicular lymphoma (tFL), Richter's Transformation;
(2) One patient with Stage II disease treated at DL3

Data as of September 28, 2020

Dose-Dependent Responses Observed with CTX110

Best response per 2014 Lugano criteria[1] by independent central assessment

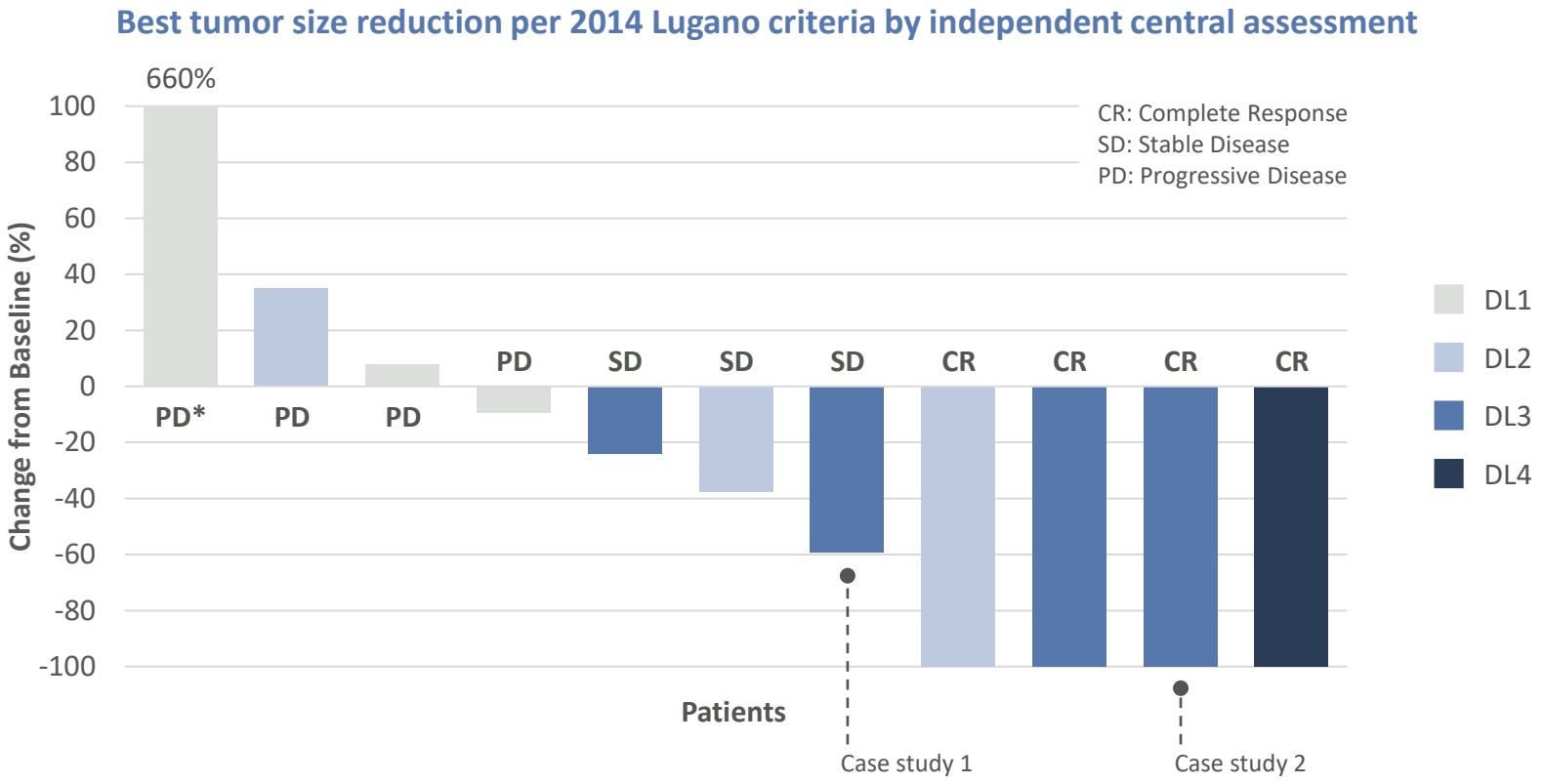
Cell dose (CAR+ T cells)	DL1 $30x10^6$ *N=3*	DL2 $100x10^6$ *N=3*	DL3 $300x10^6$ *N=4*	DL4 $600x10^6$ *N=1*
Overall response rate (ORR), N (%)	0 (0%)	1 (33%)	2 (50%)	1 (100%)
Complete response (CR) rate, N (%)	0 (0%)	1 (33%)	2 (50%)	1 (100%)

First efficacy assessment occurs at M1 visit

(1) Cheson, *et al*. *J Clin Oncol*. (2014)

Data as of September 28, 2020

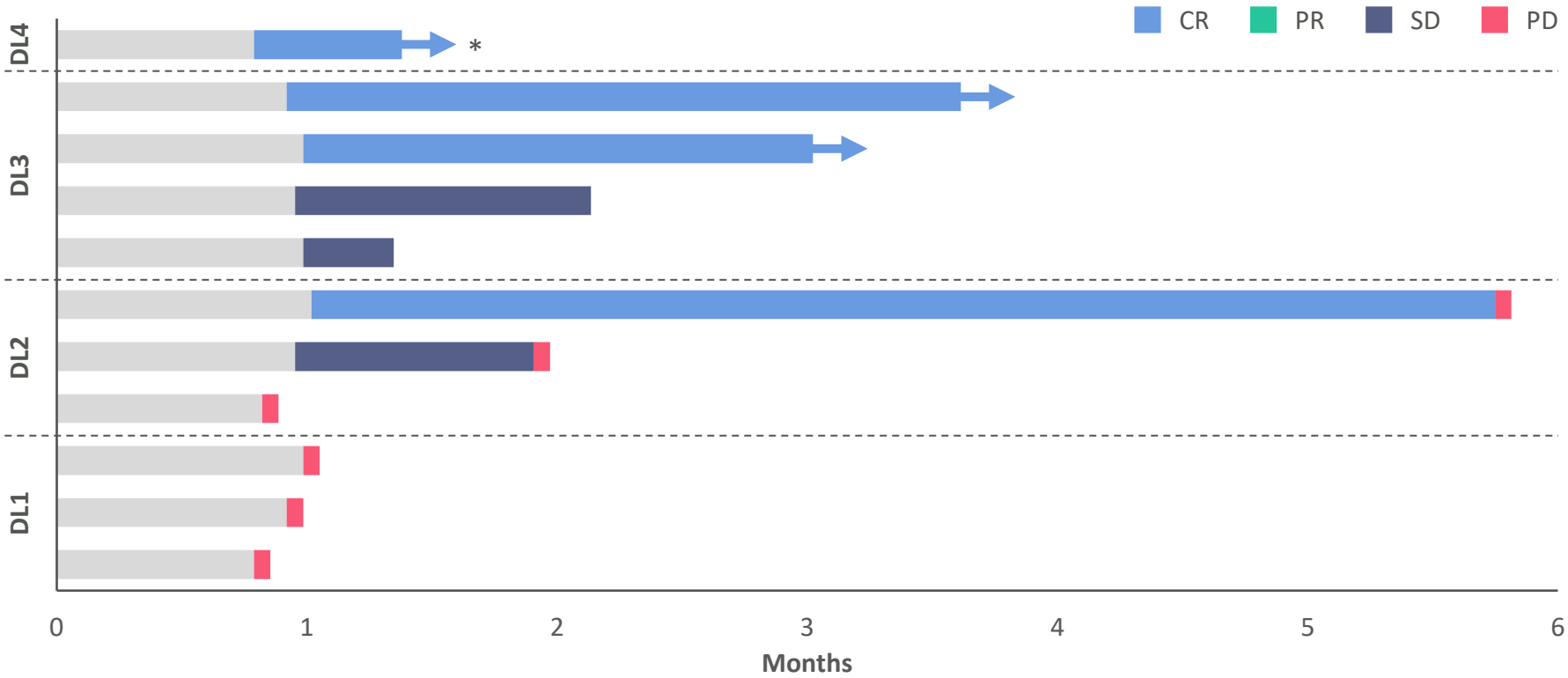
Dose-Dependent Reduction in Tumor Size with CTX110



* Patient subsequently failed autologous CAR-T

Data as of September 28, 2020

Complete Responses with CTX110 Showed Durability at Month 3 and Beyond



Imaging per protocol occurs at M1, M3, and M6; * Patient died while in CR at Day 52 post CTX110 infusion following data cutoff

Data as of September 28, 2020

Acceptable Safety Profile with CTX110 at DL3 and Below

Treatment-emergent adverse events (AEs) of special interest in DL1-3, N (%)

N=10	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Graft-versus-Host Disease (GvHD)	0	0	0	0	0
Cytokine Release Syndrome (CRS)[1,2]	1 (10%)	2 (20%)	0	0	0
ICANS[1,3]	0	1 (10%)	0	0	0
Infections	0	0	1 (10%)	0	0

For patients in DL1 through DL3 (N=10):

- **No GvHD** despite all patients with ≤3/12 HLA match to CTX110 donors
- **No CRS or ICANS above Grade 2**
- **No infusion reactions**
- **4 serious adverse events (SAEs) following CTX110 infusion not related to disease progression among 3 treated patients:** ICANS (n=1), CRS (n=1), periorbital cellulitis (n=1), febrile neutropenia (n=1)

(1) Per ASTCT criteria; other AEs graded per CTCAE; (2) Includes two separate episodes of CRS (1 G1, 1 G2) in single patient; worst grade reported; (3) Immune effector Cell-Associated Neurotoxicity Syndrome

Data as of September 28, 2020

Patient Treated at DL4 (600x10^6 CAR$^+$ T cells)

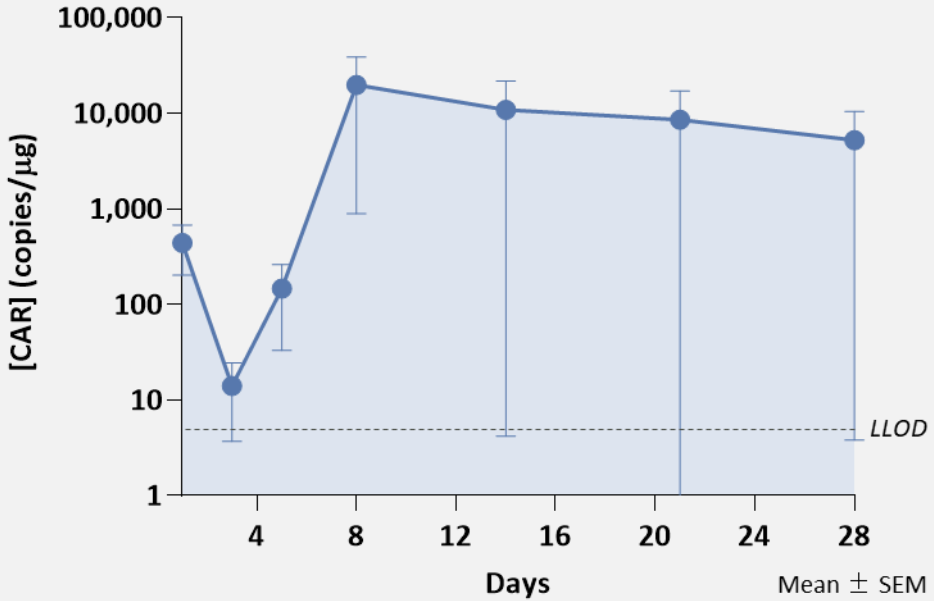
- **Patient characteristics:** 72-year-old male with relapsed transformed follicular lymphoma following five prior lines of therapy, including autologous stem cell transplant
- **Efficacy:** Complete response on Day 25 post infusion of CTX110
- **Safety:**
  - Experienced Grade 2 CRS at Day 5 that resolved
  - Admitted with febrile neutropenia at Day 26 and developed confusion and memory loss starting at Day 28, with further deterioration ultimately requiring intubation for airway protection
  - Initially treated for ICANS and later found to have reactivation of HHV-6 and HHV-6 encephalitis
  - Despite treatments, patient remained obtunded and died on Day 52 after family requested withdrawal of care

Emerging Pharmacokinetic Profile of CTX110

For patients in DL2 through DL4:

- **CAR-T cells detected at multiple time points in all patients**
- **Redistribution phase** observed from Day 1 to Day 3, followed by expansion
- **Consistent peak expansion** of CTX110 in the peripheral blood **seen around 1-2 weeks post infusion**
- **CTX110 detected out as late as 180 days** after administration

Peripheral blood CAR levels in patients treated at DL2-DL4



CTX110 Case Study: Stable Disease with Remaining Tumor Negative for CD19

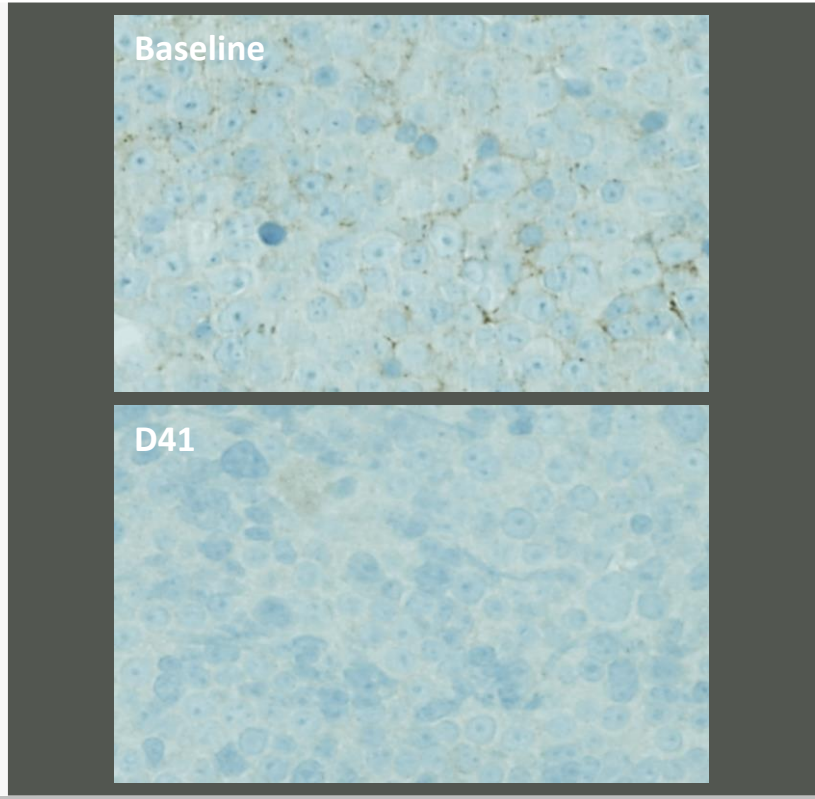
Patient characteristics

- 62-year-old male with transformed follicular lymphoma
- Relapsed following two prior lines of therapy
- Treated with CTX110 at DL3 ($300x10^6$ CAR^+ T cells)

Safety and efficacy

- No fever, CRS, or ICANS
- Visible reduction in lymph nodes on physical exam
- SD at day 28 with 59% reduction in tumor size, but remaining sites of disease were FDG avid
- Pre-treatment tumor biopsy showed positive staining for CD19 by IHC, whereas Day 41 post-CTX110 tumor biopsy did not, indicative of CD19-negative disease

IHC: Immunohistochemistry; FDG: Fluorodeoxyglucose



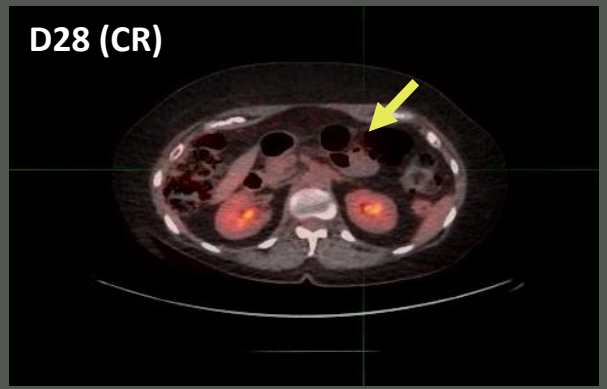
CTX110 Case Study: Complete Response Following Eradication of a Large Tumor Mass

Patient characteristics

- 62-year-old female diagnosed with DLBCL
- Relapsed following two prior lines of therapy, including autologous SCT
- Treated with CTX110 at DL3 ($300x10^6$ CAR^+ T cells)

Safety and efficacy

- CR at Day 28 with no tumor visible
- Deauville 5 to Deauville 1 for FDG uptake
- No fever, CRS, or ICANS
- CR ongoing at 3+ months



Initial CTX110 Data Supports Our Approach

Dose-dependent antitumor activity

- Early evidence of dose response
- Complete responses achieved in 4 patients (both DLBCL and tFL)
- Data in line with early autologous CAR-T trials

Acceptable safety profile at DL3 and below

- No CRS or ICANS above Grade 2 at DL3 and below; no GvHD at any dose level
- Responses achieved without the use of more toxic lymphodepletion agents, consistent with CTX110 being engineered for immune evasion

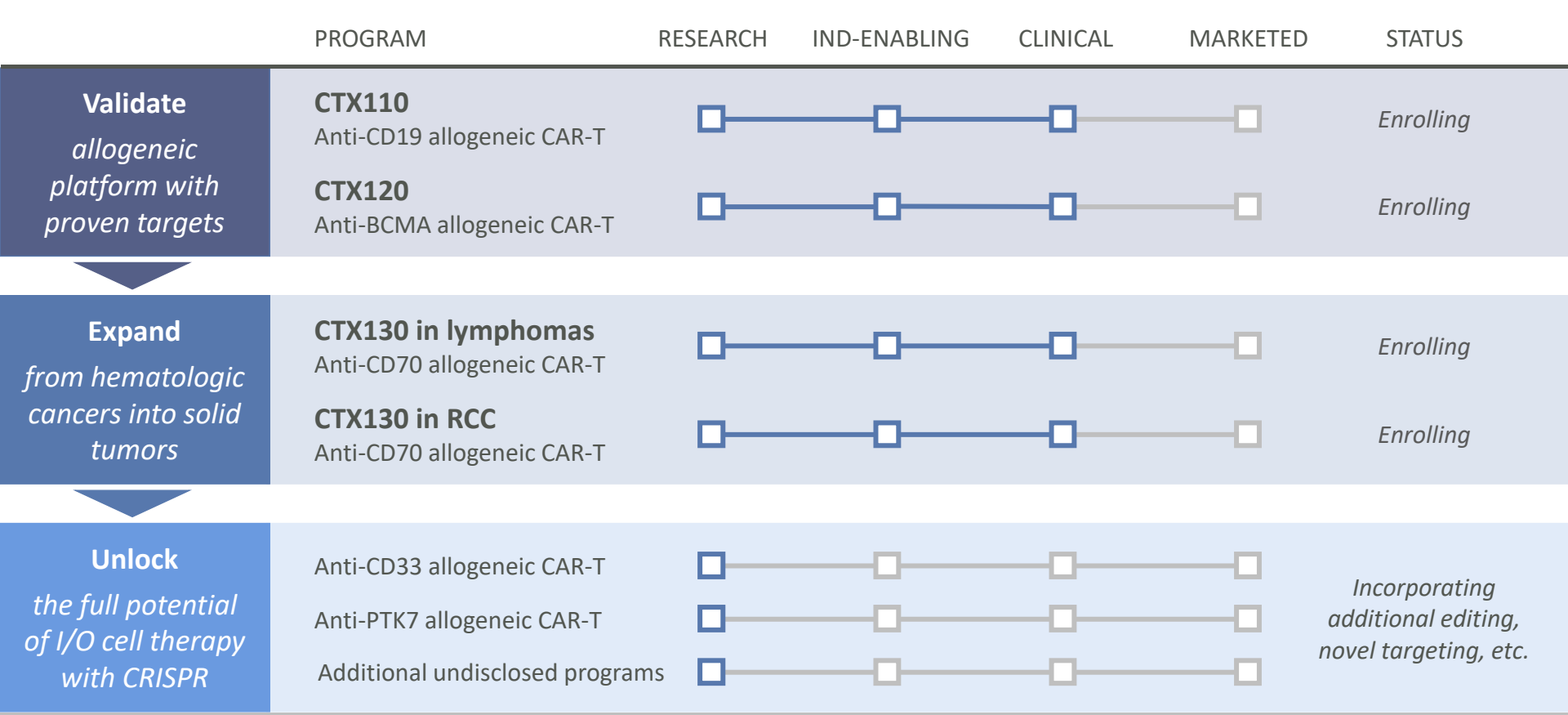
Initial experience demonstrates versatility of allogeneic CAR-T

- All enrolled patients treated rapidly – no need for bridging chemotherapy or risk of manufacturing failure
- Responses seen across multiple product lots manufactured from different donors
- Validates our CRISPR-edited allogeneic CAR-T approach

Planned Next Steps for CTX110 and Our CRISPR-Edited CAR-T Pipeline

- **"Full steam ahead" on CTX110**
  - Proceed into expansion cohort following selection of optimal dose
  - Re-dosing now included as an option in all cohorts
    - One patient (SD following initial treatment with CTX110 at DL3) re-dosed at DL3
- **Continue rapid progress on CTX120 and CTX130**
  - Dosing ongoing in trial of CTX120 in multiple myeloma
  - Dosing ongoing in trials of CTX130 in renal cell carcinoma and in T and B cell lymphomas
  - Initial data for both programs expected in 2021
- **Building on the pipeline:** announcement of additional programs planned in 2021

Our I/O Strategy and Pipeline



Thank You to Patients and Their Families

CTX110 sites

United States	▪ **University of Kansas Medical Center** *Westwood, KS* ▪ **Oregon Health and Science University** *Portland, OR* ▪ **Sarah Cannon Research Institute** *Nashville, TN* ▪ **University of Chicago** *Chicago, IL* ▪ **Mayo Clinic** *Jacksonville, FL* ▪ **Texas Transplant Institute** *San Antonio, TX*
Europe	▪ **University Medical Center Hamburg-Eppendorf** *Hamburg, Germany*
Australia	▪ **Peter MacCallum Cancer Centre** *Melbourne* ▪ **Royal Prince Alfred Hospital** *Sydney*

Thank you to patients and their families, investigators, and site staff

CRISPR Therapeutics

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