CARSGEN
THERAPEUTICS

CARsgen Therapeutics (HKEX: 02171)

April 2025

Disclaimer

THIS DOCUMENT IS FOR INFORMATIONAL PURPOSES ONLY AND IS NOT INTENDED TO BE, AND SHALL NOT BE CONSTRUED AS, AN OFFER, INDUCEMENT, INVITATION, SOLICITATION, COMMITMENT OR ADVERTISEMENT WITH RESPECT TO THE PURCHASE, SUBSCRIPTION OR SALE OF ANY SECURITY AND NO PART OF IT SHALL FORM THE BASIS OF, OR BE RELIED UPON IN CONNECTION WITH, ANY CONTRACT OR COMMITMENT WHATSOEVER.

The recipient agrees to keep the contents of the document confidential and must not reproduce or distribute the document, in whole or in part, to any person in any manner whatsoever, without the prior written consent of the Company.

Unless otherwise indicated, the information used in preparing the document was prepared by the Company or from public sources and has not been independently verified by any person. This document is for discussion purposes only and has not been prepared with a view toward public disclosure under applicable securities laws or otherwise. The contents of this document are subject to corrections or changes at any time without further notice and will not be updated to reflect material developments which may occur after the date of this document. No representation or warranty, express or implied, is made as to the fairness, accuracy, completeness or correctness of such information and nothing contained herein is, or shall be relied upon as, a representation, whether as to the past, the present or the future. None of the Company, its affiliates, directors, officers, employees, advisers, agents or representatives or any other person shall have any liability whatsoever (in negligence or otherwise) for any loss howsoever arising from any use of the contents of this document or otherwise arising connection therewith.

This document is not intended to provide the basis for evaluating and should not be considered a recommendation with respect to, any transaction or other matter. Any analyses included herein are not and do not purport to be appraisals of the assets or business of the Company or any of its subsidiaries or affiliates. Nothing in this document should be construed as regulatory, valuation, legal, tax, accounting or investment advice. Before you enter into any transaction, you should ensure that you will be responsible for conducting your own due diligence investigation with respect to the Company and fully understand the potential risks and rewards of that transaction and you should consult with such advisers as you deem necessary to assist you in making these determinations, including, but not limited to, your accountants, investment advisors and legal and/or tax experts. Any decision to purchase securities of the Company in any public or private offering should be made solely on the basis of the prospectus and/or international offering circular to be prepared by the Company in relation to any such contemplated offering together with any supplementary pricing information. This document contains no information or material which may result in it being deemed (1) to be a prospectus within the meaning of section 2(1) Companies (Winding Up and Miscellaneous Provisions) Ordinance (Chapter 32 of the Laws of Hong Kong) (the “Companies Ordinance”), or an advertisement in relation to a prospectus or proposed prospectus or extract from or abridged version of a prospectus within the meaning of section 38B of the Companies Ordinance or an advertisement, invitation or document containing an advertisement or invitation falling within the meaning of section 103 of the Securities and Futures Ordinance (Chapter 571 of the Laws of Hong Kong) (the “Securities and Futures Ordinance”) or (2) in Hong Kong to have effected an offer to the public without compliance with the laws of Hong Kong or being able to invoke any exemption available under the laws of Hong Kong, and is subject to material change without notice.

This document contains forward-looking statements that express the Company’s current views, projections, beliefs and expectations with respect to future events as of the respective dates indicated herein. Such forward-looking statements are based on a number of assumptions and factors beyond the Company’s control. As a result, they are subject to significant risks and uncertainties and actual events or results may differ materially from these forward-looking statements and the forward-looking events discussed in this document might not occur. No representation or warranty is given as to the achievement or reasonableness of, and no reliance should be placed on, any projections, targets, estimates or forecasts contained in this document.

This document is not an offer for sale of or a solicitation of an offer to buy securities in the United States or in any other jurisdiction. Securities may not be offered or sold in the United States absent registration or an available exemption from registration under the U.S. Securities Act of 1933, as amended (the “U.S. Securities Act”).

By reading this document and attending the presentation, you agree to be bound by the foregoing restrictions, and you shall be deemed to have represented to us that you (and any customers you represent) are either (a) a qualified institutional buyer (as defined in Rule 144A under the U.S. Securities Act) or (b) outside the United States (within the meaning of Regulation S under the U.S. Securities Act). You also represent that you (and any customers you represent) are “professional investors” described in Part I of Schedule 1 to the Securities and Futures Ordinance and any subsidiary legislation thereunder (including but not limited to the Securities and Futures (Professional Investor) Rules (Chapter 571D of the Laws of Hong Kong)).

We Develop Innovative and Differentiated Cell Therapies to Make Cancer and Other Diseases Curable

1

Marketed product:
- zevorcabtagene autoleucel (zevor-cel, CT053)

3

CAR-T Products at IND stage:
- Satri-cel (Claudin18.2)
- CT011 (GPC3)
- CT071 (GPRC5D)

4+

Core technology platforms:
- CycloCAR®, THANK-uCAR®, THANK-u Plus™, LADAR®, CARcelerate®

300+

Patents (including 129 issued, as of December 31, 2024)

2

Manufacturing sites:
- Shanghai, China
- Durham, US

10+ years

Focus on innovative CAR-T therapies since company initiation

Global Reach with Integrated R&D and Manufacturing Capabilities Complemented with Synergistic Partnership

Shanghai

Headquarter, research, clinical development, GMP commercial and clinical manufacturing facility

Durham, North Carolina

CGMP manufacturing facility

Partnerships

华东医药股份有限公司 HUADONG MEDICINE CO.,LTD.

(SZ: 000963)

Exclusive commercialization of zevor-cel in mainland China

moderna

(NASDAQ: MRNA)

Evaluate satri-cel in combination with an mRNA Cancer Vaccine

inno.N

(KOSDAQ: 195940)

License of zevor-cel and CT032 in the Republic of Korea

Continuous Innovation and Technology Advancement to Tackle the Major Challenges with CAR-T therapies Since 2014

Allogeneic CAR-T

- THANK-uCAR®, THANK-u Plus™ platforms

Autologous CAR-T

- BCMA CAR-T (zevor-cel)
- first-in-class Claudin18.2 CAR-T (satri-cel)
- first-in-class GPC3 CAR-T (CT011)

Enabling Technologies

CycloCAR®
(co-expression of IL-7 + CCL21)

LADAR®
(precise targeting)

Lymphodepletion
(FNC regimen)

Binder
(humanized/fully-human antibodies against ~20 targets)

Competitive Product Pipeline with Global Rights

	Product Candidate[1]	Target	Indication	Pre-clinical / Phase I / Phase II/III[2] / BLA NDA
Autologous CAR-T	**Zevor-cel (CT053)[3]**	BCMA	R/R MM	LUMMICAR 1 (China) — launched
			R/R MM	LUMMICAR 2 (US, Canada)
	Satri-cel (CT041)	Claudin18.2	GC/GEJ	ST-01 (China)
			GC/PC	ST-02 (US, Canada)
			PC (adjuvant)	ST-05 (China)
			GC/GEJ, PC, etc.	IIT (China)
			GC/GEJ (adjuvant)	IIT (China)
	CT071	GPRC5D	R/R MM, R/R pPCL	(US)
			R/R MM, R/R PCL	IIT (China)
			NDMM	IIT (China)
	CT011	GPC3	HCC (adjuvant)	(China)
Allogeneic CAR-T	**CT0590[4]**	BCMA	R/R MM, R/R PCL	IIT (China)
	CT059X	BCMA	R/R MM, R/R PCL	IIT (China)
	KJ-C2219	CD19/CD20	B-cell malignancies	IIT (China)
			SLE, SSc	IIT (China)
	KJ-C2320	CD38	AML	IIT (China)
	KJ-C2114	Undisclosed	Solid tumors	
	KJ-C2526	NKG2DL	AML, other malignancies, senescence	

[1] All product candidates are self-developed with global rights
[2] Phase II trials of some indications are pivotal studies
[3] Core Product Candidate. Commercial rights in mainland China have been granted to Huadong Medicine (SZ: 000963). Rights in the South Korean market have been licensed out to HK Inno.N (KOSDAQ: 195940)
[4] CT0590 enrollment finished

for hematologic malignancies; for solid tumors; for autoimmune diseases

R/R MM: relapsed / refractory multiple myeloma; GC: gastric cancer; GEJ: gastroesophageal junction cancer; PC: pancreatic cancer; HCC: hepatocellular carcinoma; R/R pPCL: relapsed/refractory primary plasma cell leukemia; NDMM: newly diagnosed multiple myeloma; SLE: systemic lupus erythematosus; SSc: systemic sclerosis; AML: acute myeloid leukemia

Autologous CAR-T Against Hematologic Malignancies

CARSGEN
THERAPEUTICS

Zevor-cel: Differentiated Fully-human BCMA CAR-T for R/R MM (Approved in China)

Zevor-cel Highlights

- Optimized scFv
- Enhanced binding affinity
- High stability
- Enhanced anti-tumor activity
- Excellent safety profile
- Co-stimulatory domain: 4-1BB
- Low immunogenicity

✓ Designations: RMAT (FDA), Orphan Drug (FDA)

✓ NDA approved by China NMPA (February 23, 2024)

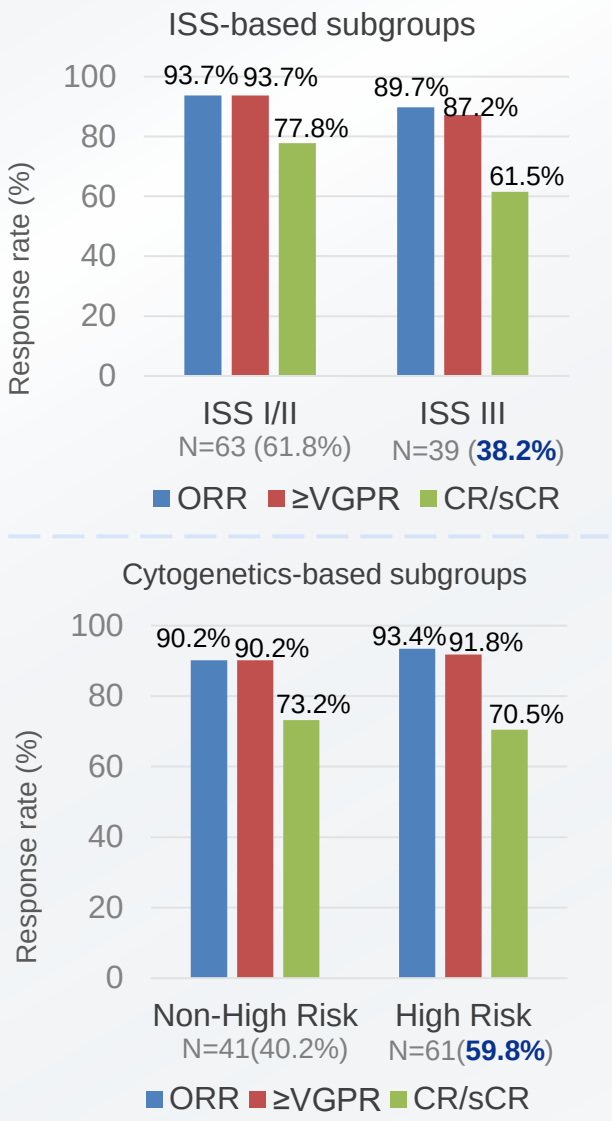
China Pivotal Phase II (LUMMICAR-1) [1]
N=102

Follow-up, median (range), Month	20.3 (0.4-27)
ISS stage III, No. (%)	39 (38.2%)
High risk Cytogenetic, No. (%)	61 (59.8%)
EMD+ , No. (%)	11 (10.8%)
Prior lines of therapies, median (range)	4 (3-15)
Double-class refractory*, No. (%)	91 (89.2%)
Triple-class refractory**, No. (%)	23 (22.5%)
ORR, No. (%)	94 (92.2%)
CR/sCR, No. (%)	73 (71.6%)
≥VGPR, No. (%)	93 (91.2%)
mDoR, Month	Not mature
mPFS, Month	Not mature
MRD negative***, No. (%)	73 (100%)
≥Grade 3 CRS, No. (%)	7 (6.9%)
≥Grade 3 NT, No. (%)	0
Treatment related death, No.	1

*Double-class refractory: Refractory to a proteasome inhibitor and immunomodulatory drug
**Triple-class refractory: Refractory to a proteasome inhibitor, immunomodulatory drug and anti-CD38 antibody
***In the patients achieved CR/sCR

1. Chen W, et al. EHA 2024. 2024 Jun; Oral presentation S209

Zevor-cel: Outstanding Efficacy and Manageable Safety



Long-term survival with deep response

It has been reported that ISS-III and high risk cytogenetics could impact the efficacy of BCMA CAR-T. Although, zevor-cel treated a high percentage of patients at ISS III stage or high risk cytogenetics in pivotal phase II, it showed competitive efficacy (left figures).

◆ Overall Superior efficacy

- IIT[1]: ORR of 87.5%, sCR/CR rate of 79.2%.
- Phase I[2]: **2-year OS rate of 100%, 3-year OS rate of 92.9%.**
- Pivotal phase II[3,4]: ORR of 92.2%, predicted **30-month OS rate** of **87.7%** (in patients who achieved CR/sCR) .

Higher safety, lower incidence of SAE

◆ In IIT, Phase I, and Phase II studies

- ≥Grade 3 CRS incidence: 0%, 0%, 6.9%, respectively.
- ≥Grade 3 neurotoxicity incidence: 4.2%, 0%, 0%, respectively.
- Treatment-related death: 0%, 0%, 1%, respectively.

◆ Low incidence of ≥Grade 3 infections or prolonged hematologic toxicity

- Low incidence of ≥Grade 3 infections.
- Significantly low incidence of ≥Grade 3 prolonged (>30 days) cytopenia.

1. Yang M, et. al. *Haematologica*. 2022 Aug 1;107(8):1960-1965
2. Fu C, et. al. ASH 2023. 2023 Dec; Poster #4845
3. Chen W, et al. EHA 2024. 2024 Jun; Oral presentation S209
4. Chen W, et al. [poster]. 2024 ASH. 2024 Dec; Poster 4762

CT071: Differentiated GPRC5D CAR-T with CARcelerate® Platform

Product

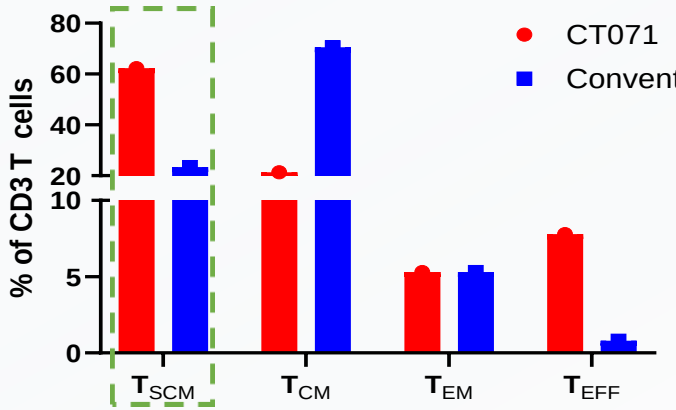
- Fully-human scFV generated by CARsgen
- For relapsed R/R Multiple Myeloma or R/R Primary Plasma Cell Leukemia
- Proprietary **CARcelerate®** platform

Manufacturing Time:

CARcelerate®: **~30 hours**

Conventional: **> 7 days**

Younger, healthier, possibly more potent CAR-T



Clinical Development Status

- China investigator-initiated trial for R/R MM and PCL (NCT05838131) **Enrollment Completed**
- China investigator-initiated trial for NDMM (NCT06407947) **Enrollment Completed**

- **IND cleared:** R/R MM or R/R pPCL

CT071: Baseline Characteristics

Patient Characteristics	0.1×10^6 cells/kg (n=8)	0.3×10^6 cells/kg (n=9)	All Patients (n=17)
R-ISS disease stage, No. (%)			
II	4 (50.0)	8 (88.9)	12 (70.6)
III	4 (50.0)	0	4 (23.5)
ECOG PS, No. (%)			
1	4 (50.0)	5 (55.6)	9 (52.9)
2	1 (12.5)	0	1 (5.9)
Extramedullary Disease [a], No. (%)	2 (25.0)	2 (22.2)	4 (23.5)
High-risk cytogenetics, No. (%)	6 (75.0)	6 (66.7)	12 (70.6)
Prior Lines of Therapy, median (range)	4 (1, 12)	5 (3, 7)	5 (1, 12)
Prior CAR T, No. (%)	2 (25.0)	2 (22.2)	4 (23.5)
Prior ASCT, No. (%)	2 (25.0)	7 (77.8)	9 (52.9)
Double-class Refractory [b], No. (%)	7 (87.5)	9 (100)	16 (94.1)
Triple-class Refractory [c], No. (%)	4 (50.0)	7 (77.8)	11 (64.7)

Note, a) defined as soft tissue or paramedullary plasmacytomas; b) Double-class: one or more proteasome inhibitor, and one or more immunomodulatory drug; c) Triple-class: one or more proteasome inhibitor, one or more immunomodulatory drug, and one or more anti-CD38 antibody.

Abbreviations: R-ISS, Revised International Staging System; ECOG PS, Eastern Cooperative Oncology Group Performance Status; ASCT, Autologous Stem Cell Transplantation.

*Cut-off date: June 21, 2024

1. Du J, et al. 2024 ASH. 2024 Dec; Poster 3451

CT071: Early and Deep Responses with Promising Safety Profile

	0.1×10⁶ cells/kg (n=8)	0.3×10⁶ cells/kg (n=9)	All Patients (n=17)
ORR, No. (%)	8 (100)	8 (88.9)	16 (94.1)
CR/sCR rate, No. (%)	5 (62.5)	4 (44.4)	9 (52.9)
VGPR or better rate, No. (%)	5 (62.5)	5 (55.6)	10 (58.8)
Time to CR or better, Median (range), Month	1 (1.0, 1.1)	1.9 (1.0, 4.3)	1 (1.0, 4.3)
MRD Negativity ($<10^{-6}$) in BM, No. (%)	8 (100)	7 (77.8)	15 (88.2)
MRD negativity ($<10^{-6}$) with CR/sCR subjects*, No. (%)	5 (100)	4 (100)	9 (100)
CRS, No. (%)	6 (75.0)	5 (55.6)	11 (64.7)
Grade 1, No. (%)	5 (62.5)	3 (33.3)	8 (47.1)
Grade 2, No. (%)	1 (12.5)	2 (22.2)	3 (17.6)
ICANS, No. (%)	0	0	0
Onychomadesis, No. (%)	4 (50.0)	0	4 (23.5)
Skin rash, No. (%)	0	1 (11.1)	1 (5.9)
AE leading to death, No. (%)	0	0	0

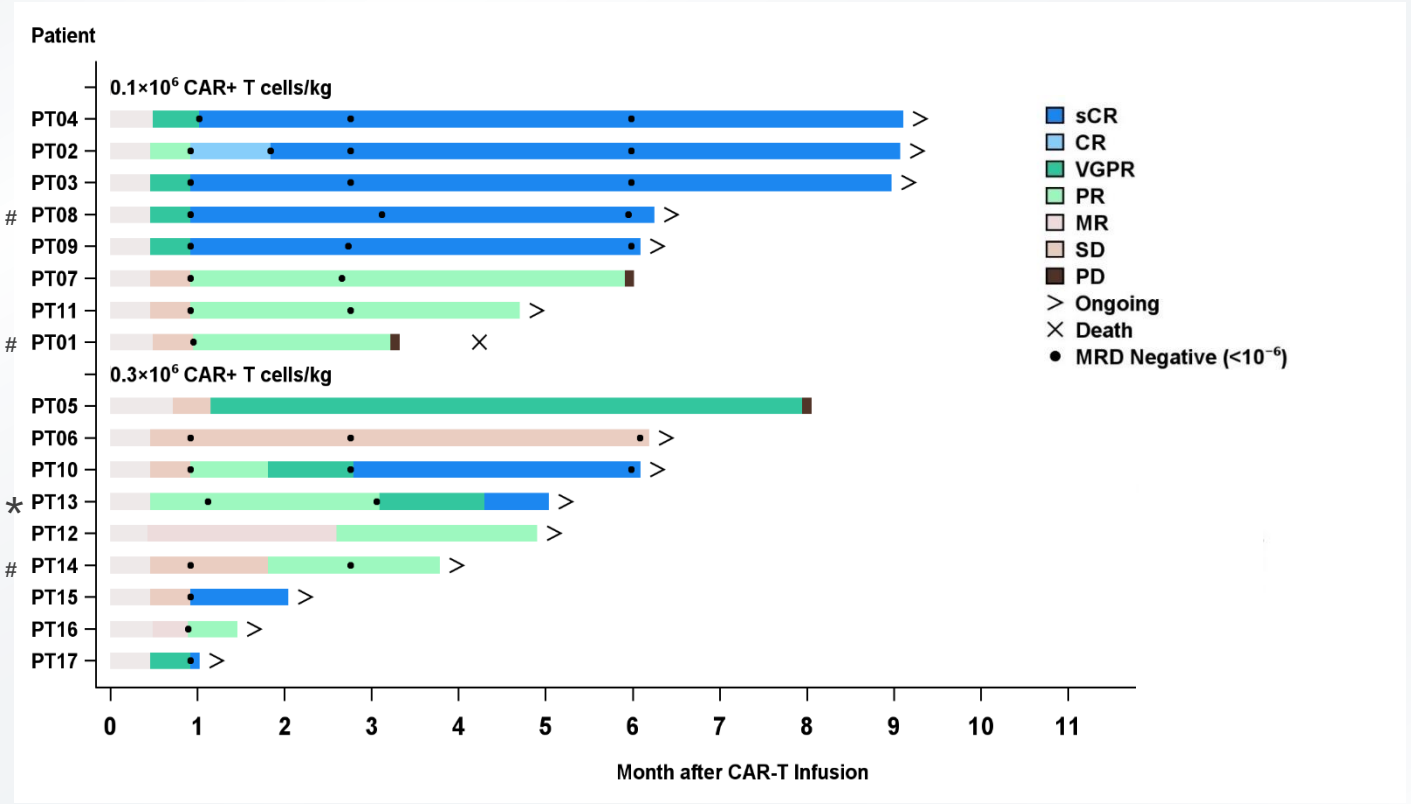
Abbreviations: CI, Confidence Interval; CR, Complete Response; DOR, Duration of Response; MRD, Minimal Residual Disease; NA, Not Applicable; ORR, Objective Response Rate; PR, Partial Response; sCR, Stringent Complete Response; SD, Stable Disease; VGPR, Very Good Partial Response; TRAE, Treatment-related Adverse Event; SAE, Serious Adverse Event; CRS, Cytokine Release Syndrome; ICANS, Immune Effector Cell-associated Neurologic Syndrome.

*Percentages were calculated based on CR/sCR patients (n=9)

*Cut-off date: June 21, 2024

1. Du J, et al. 2024 ASH. 2024 Dec; Poster 3451

CT071: Rapid and Durable Responses



- Seven patients achieved CR or better at week 4.
- All 4 patients with previous exposure to BCMA or BCMA/CD19 CAR-T responded (2 sCR and 2 PR).
- One patient with SD demonstrated ongoing tumor shrinkage of a large EMD (125 mm×99 mm at baseline) with 38.2% decrease at week 26, along with 93.0% decrease in serum M protein from baseline.

Note:
* Previous exposure to BCMA CAR-T.
# Previous exposure to BCMA/CD19 CAR-T.

*Cut-off date: June 21, 2024

1. Du J, et al. 2024 ASH. 2024 Dec; Poster 3451

Autologous CAR-T Against Solid Tumors

CARSGEN THERAPEUTICS

Unmet Medical Needs in Solid Tumors, Including Gastric and Pancreatic Cancers

Gastric Cancer 	Incidence ~25.6K[1] • Resectable ~10.0K Mortality ~11.0K[1]	Incidence ~358.7K[1] • Resectable ~300.0K Mortality ~260.4K[1]
	5-year survival rate of advanced GC is 5-20%; For advanced GC (3L+), ORR is 4.5%, mPFS < 2months, mOS < 6 months (TAGS study)[2]	
Pancreatic Cancer 	Incidence ~60.1K[1] Mortality ~49.5K[1]	Incidence ~118.7K[1] Mortality ~106.3K[1]
	5-year survival rate of PC is about 10%; No effective SOC for PC (2L+)	

1. International Agency for Research on Cancer. Population factsheets. 2022
2. Shitara K, et al. *Lancet Oncol.* 2018 Nov;19(11):1437-1448

CARsgen Proprietary Claudin18.2 IHC Test

Claudin18.2 IHC test kit with high sensitivity

Gastric Cancer

Medium & high positivity rate

(≥2+, ≥40%)

68%

Pancreatic Cancer

Medium & high positivity rate

(≥2+, ≥40%)

55%

Bile Duct Cancer

Medium & high positivity rate

(≥2+, ≥40%)

25%

Satri-cel (CT041): Global First-in-Class CAR-T for Claudin18.2-Positive Solid Tumors

Product

- **Optimized scFv[1]**
  - ✓ High binding affinity
  - ✓ High stability

- Innovative FNC (FC + low-dose **Nab-Paclitaxel**) preconditioning regimen to enhance penetration and anti-tumor effect of CAR-T cells

Designations

- **RMAT** (FDA)
- **Orphan Drug** (FDA)
- **Breakthrough Therapy** (NMPA)

Collaboration

CARsgen and Moderna, Inc. (Nasdaq: MRNA) have initiated a collaboration agreement to investigate satri-cel in combination with Moderna's investigational Claudin18.2 mRNA cancer vaccine

Clinical Development Plan

- GC (3L+) confirmatory Phase II trial in China: **Enrollment completed**; **positive topline results**; **plan to submit the NDA in H1, 2025**
- PC adjuvant therapy Phase I trial in China: **Ongoing**
- GC adjuvant therapy IIT in China: **Ongoing**

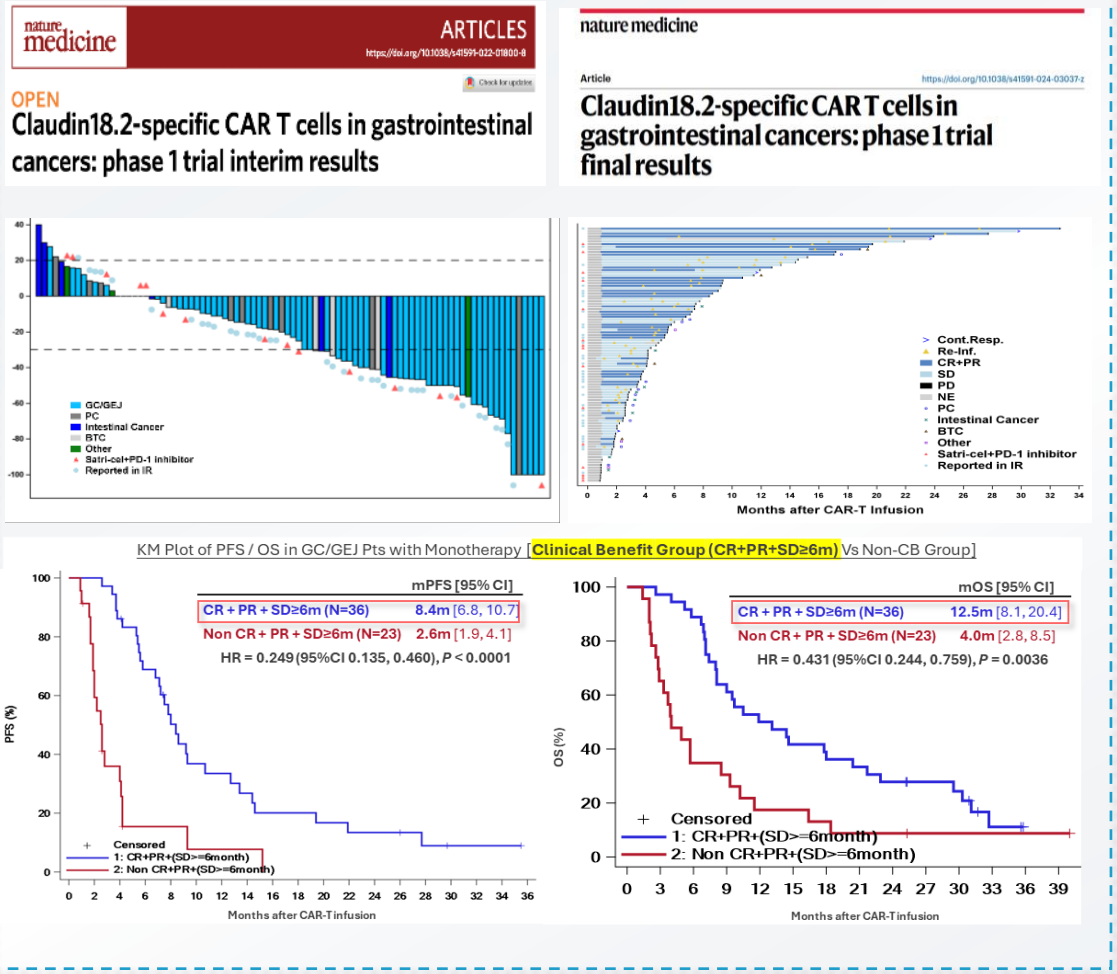
Expansion of clinical development in
- earlier lines of therapy
- additional Claudin18.2 positive cancers

1. Jiang H, et al. *J Natl Cancer Inst.* 2019;111(4):409-418

Breakthrough Efficacy of Satri-cel in Later-Line Therapy for GC/GEJ

	ORR	mPFS | mOS (month)
CT041	55%	5.8 | 9.0
Immunotherapy	11%	1.6 | 5.2
Chemotherapy, Targeted Therapy	<5%	<2 | <6

Presentations at international conferences and publications in top-tier journals



1. Qi C, et. al. *Nat Med*. 2022 Jun;28(6):1189-1198.
2. Qi C, et. al. *Nat Med*. 2024 Aug;30(8):2224-2234.

Satri-cel: Clinical Data from China and the United States

	China investigator-initiated trial (NCT03874897)[1,2]	Phase Ib/II in China (NCT04581473)[3]	Phase 1b in the US (NCT04404595)[4]	
Sample size, No.	51 GC/GEJ*	14 GC/GEJ	7 GC/GEJ	12 PC
Median follow-up, Month	32.4*	8.8	8.9	
ORR	54.9%*	57.1%	42.9%	16.7%
mPFS, Month	5.8**	5.6	5.7	2.7
mDoR, Month	6.4*	Not reported	6.9	3.4
mOS, Month	9.0**	10.8	8.9	8.9
≥Grade 3 CRS, No.	0	1***	0	2
≥Grade 3 ICANS, No.	0	0	0	
Treatment related death, No.	0	0	0	

*51 GC/GEJ patients with target lesions at baseline received satri-cel monotherapy.
**59 GC/GEJ patients received satri-cel monotherapy.
***One patient was related to the investigational disease (lung metastasis of GC) and fully recovered after corticosteroids treatment.

1. Qi C, et al. 2024 ASCO Abstract #2501
2. Qi C, et al. *Nat Med* (2024). https://doi.org/10.1038/s41591-024-03037-z2
3. Qi C, et. al. ASCO 2022. 2022 Jun; Abstract #4017
4. Botta G, et. al. ASCO GI 2024. 2024 Jan; Abstract #356

Satri-cel: Extension to GC/PC Earlier Line Treatment

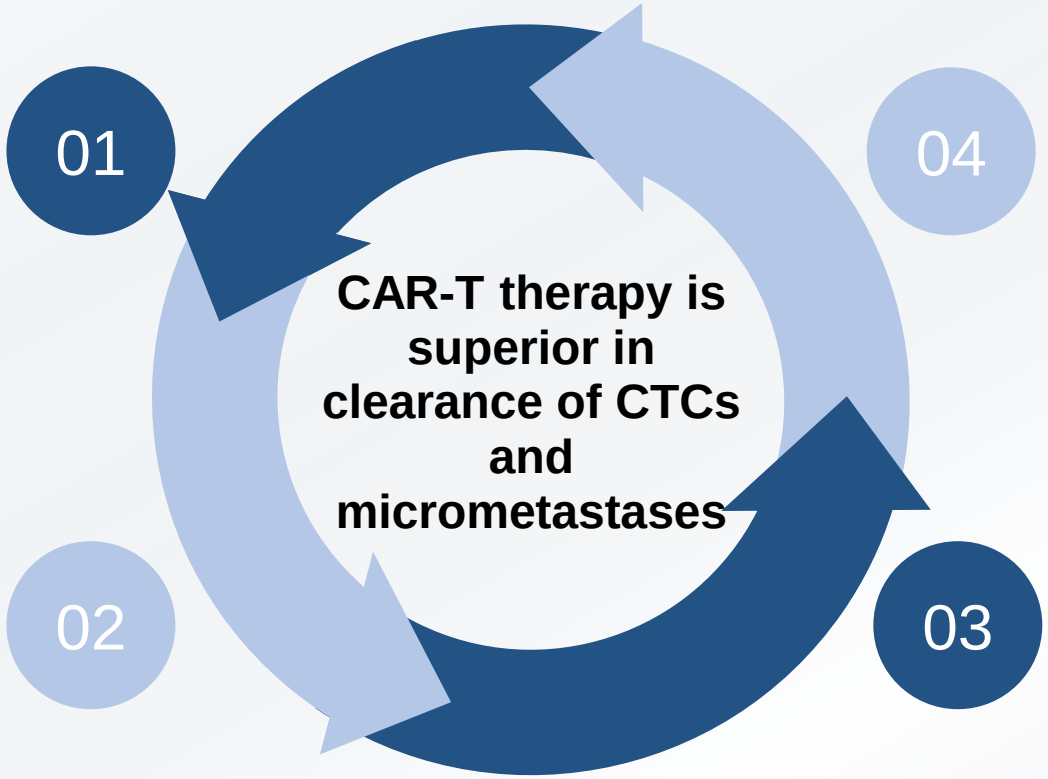
Promising great clinical value in earlier line / earlier disease stage and providing better chances of cure for a much broader patient population

More Accessible Tumor

- Low disease burden & aggressiveness
- Easier tissue penetration

Preserved Immune System

- Better quality of T cells
- More durable responses are expected



Better Tolerability

- Mild CRS
- Good hematopoietic and end-organ function

Favorable TME

- ECM & normal fibroblasts not affected by previous anti-cancer therapy

CT041 as 1L Consolidation Delivered 100% Response Rate

No.	Age/Gender	BOR of 1st line	BOR of CT041	TTR
1	**50/F**	**SD**	**PR**	**W4**
2	**55/F**	**PR**	**PR**	**W4**
3	30/F	SD	**PR**	W4
4	48/M	SD	**NN**	No target lesion
5	53/F	NE (intolerable to chemo, myelosuppression)	**PR**	W4

CT041 Efficacy Highlights

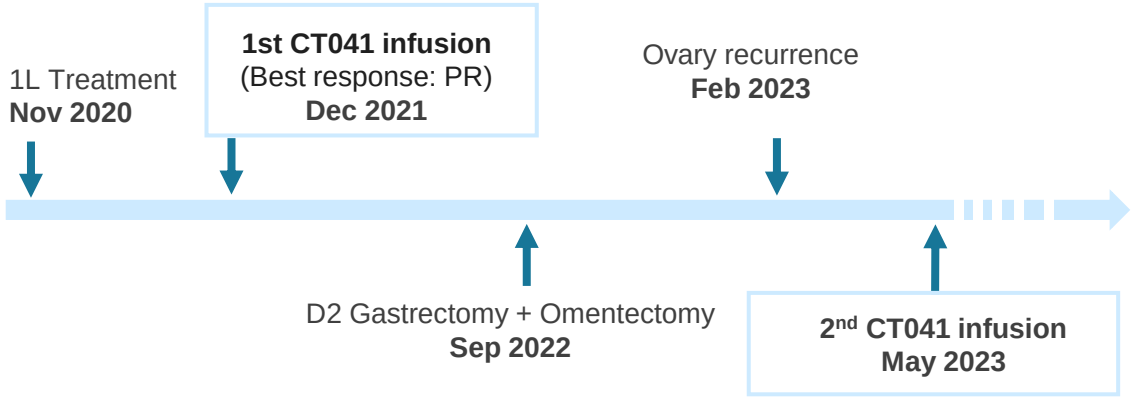
- **ORR 100%** in 4 patients with target lesions, TTR (Time-To-Response) Week 4
- 1 NN patient remained stable **beyond 15 months**
- 2 pts subsequently underwent **surgical resection** after satri-cel infusion**, and remain alive until now.**

Following CT041 Infusion, Two Patients Underwent Surgical Resection, and Remain in Long-term Survival at the Latest Follow-up

Case 1

1L Treatment

- Regimen: POS regimen (6 cycles) + S-1/Paclitaxel/TNF intraperitoneal perfusion (4 cycles)
- 1L BOR : SD

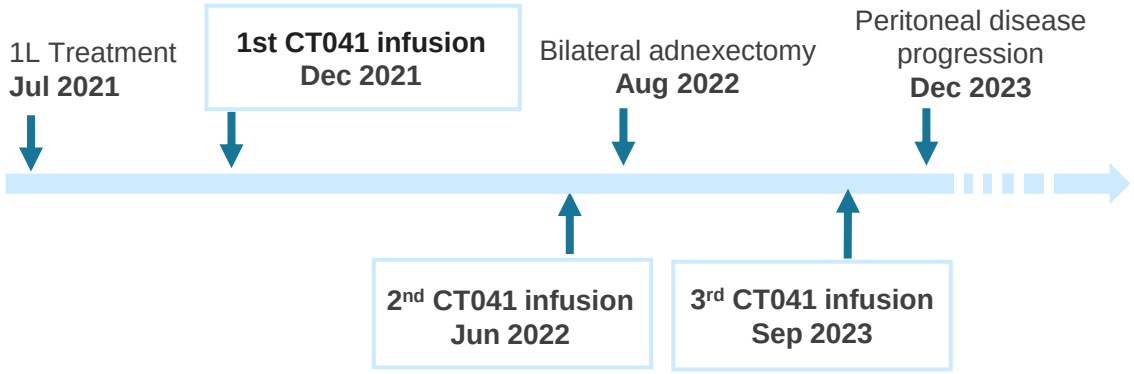


OS: 36.0+ months (last FU: Dec2024)

Case 2

1L Treatment

- **Regimen:** SOX regimen (4 cycles)
- **BOR** : PR



OS: 39.0+ months (last FU: Mar2025)

Liver Cancer: The Third Leading Cause of Cancer Mortality Worldwide

2022 Liver Cancer Epidemiology in the US and China[1]

Incidence	~43.5K
Mortality	~30.9K

Incidence	~367.7K
Mortality	~316.5K

Liver Cancer 5-year survival rate

	Global[2]	US[3]	China[4]
Liver Cancer, all stages	18%	20%	12%

1. International Agency for Research on Cancer. Population factsheets. 2022
2. Lin L, et al. *Liver Cancer*. 2020 Sep;9(5):563-582
3. 2022 American Cancer Society medical information
4. Zheng R, et al. *Chinese Journal of Cancer Research*, 2018 Dec;30(6):571-579

CT011: First-in-class CAR-T in Hepatocellular Carcinoma with PoC Clinical Results

GPC3: high expression and specificity

- Overexpression in hepatocellular carcinomas (HCC), and is associated with poor disease prognosis

CARsgen's GPC3 IHC test kit

Expression* in HCC:

70.7%

- overexpressed in other cancer types, e.g. >60% of lung squamous cell carcinoma (SCC)

CT011

Product

✓ an autologous GPC3 CAR-T product

Clinical Development

- Phase I trial **Completed**
- Phase I trial for stage IIIa HCC at high risk of recurrence after surgical resection **Ongoing**

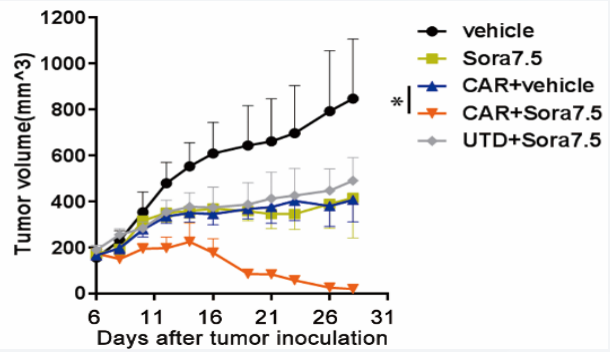
*CARsgen internal data

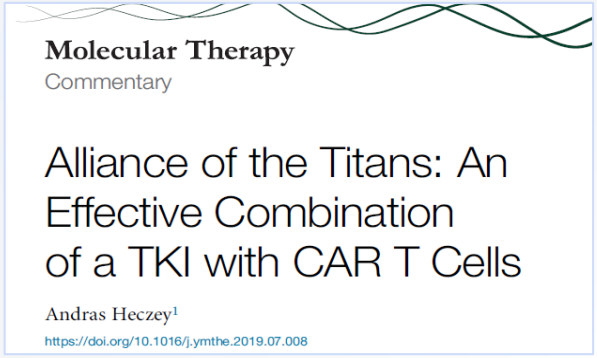
CAR-T in Combination with Small Molecules Against HCC: First publication in *Molecular Therapy*

Mol Ther. 2019 Aug 7;27(8):1483-1494. doi: 10.1016/j.ymthe.2019.04.020. Epub 2019 Apr 29.

Combined Antitumor Effects of Sorafenib and GPC3-CAR T Cells in Mouse Models of Hepatocellular Carcinoma

Xiuqi Wu [1], Hong Luo [2], Bizhi Shi [1], Shengmeng Di [1], Ruixin Sun [1], Jingwen Su [1], Ying Liu [1], Hua Li [1], Hua Jiang [3], Zonghai Li [4]





frontiers | Frontiers in Immunology

TYPE Case Report
PUBLISHED 17 August 2022
DOI 10.3389/fimmu.2022.963031

Long term complete response of advanced hepatocellular carcinoma to glypican-3 specific chimeric antigen receptor T-Cells plus sorafenib, a case report

As of Dec 2021 (last follow-up at publication)

- CR status has been over 24 months and continues

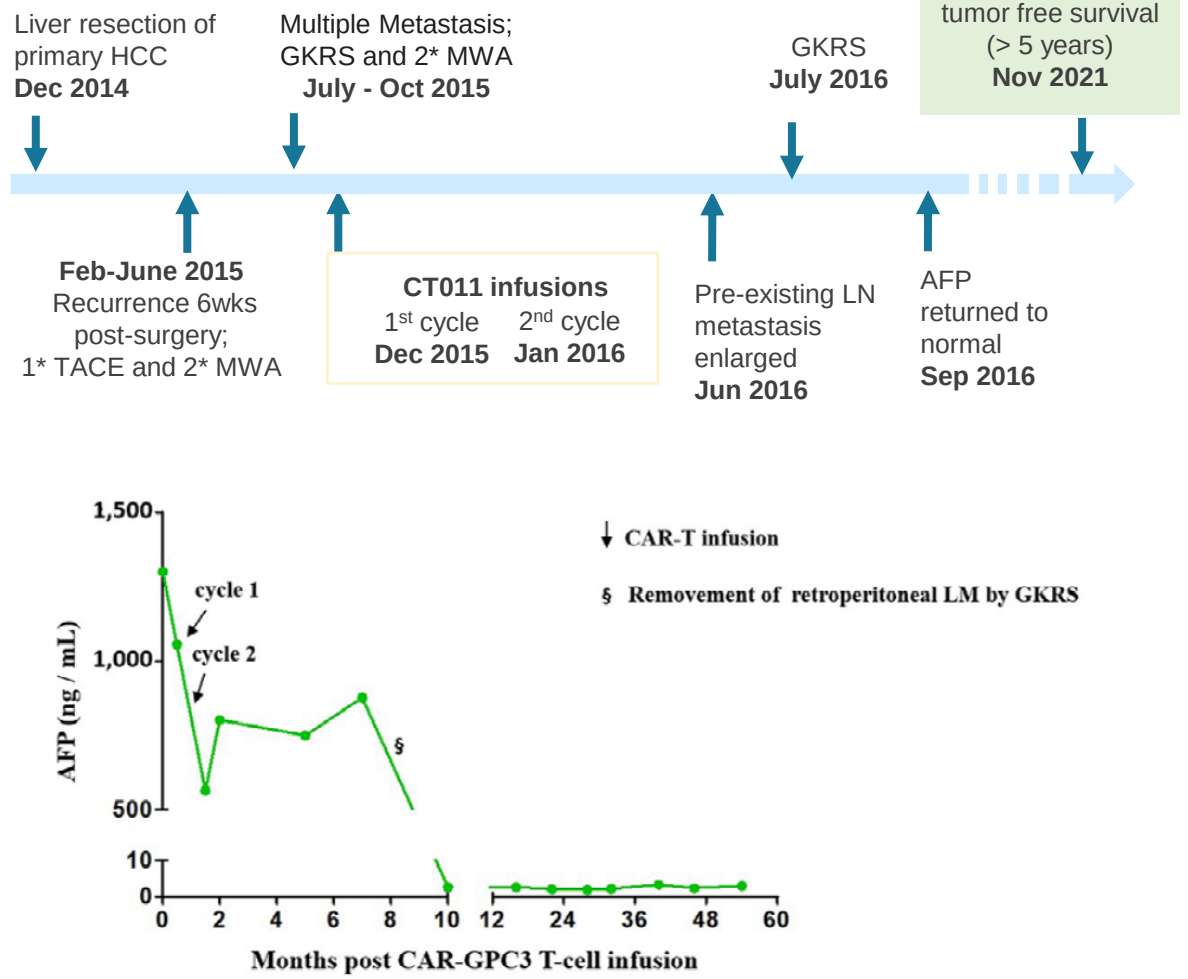
(Photo taken in Jun 2023)

1. Wu X, *Mol Ther.* 2019 Aug 7;27(8):1483-1494

CAR-T in Combination with Local Therapy Against HCC: Cover Story in *Cancer Communications*, Highlighting Two Cases of Disease-free Survival over 7 Years

Patients stayed tumor free till latest follow-up on Sep 4th, 2023

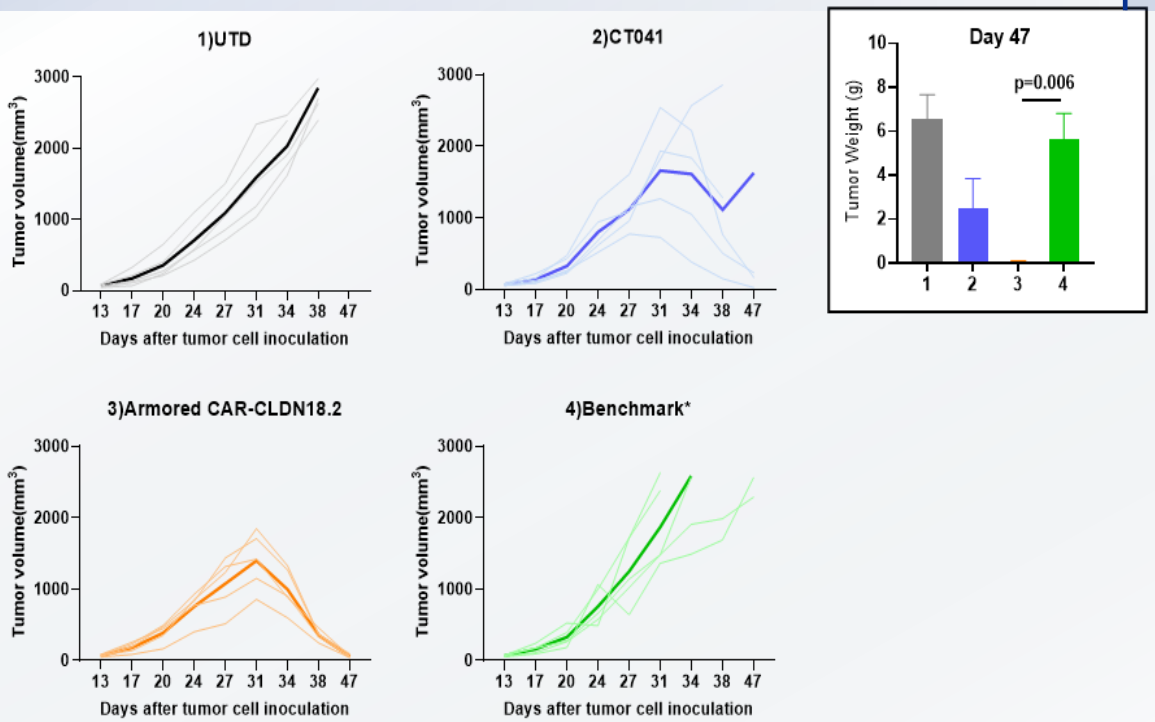
- 54-year-old male with Ib-stage HCC
- Multifocal lesions in the liver, IVCTT, and retroperitoneal lymphatic metastasis;
- Previously treated with surgical resection, TACE and MWA, GKRS



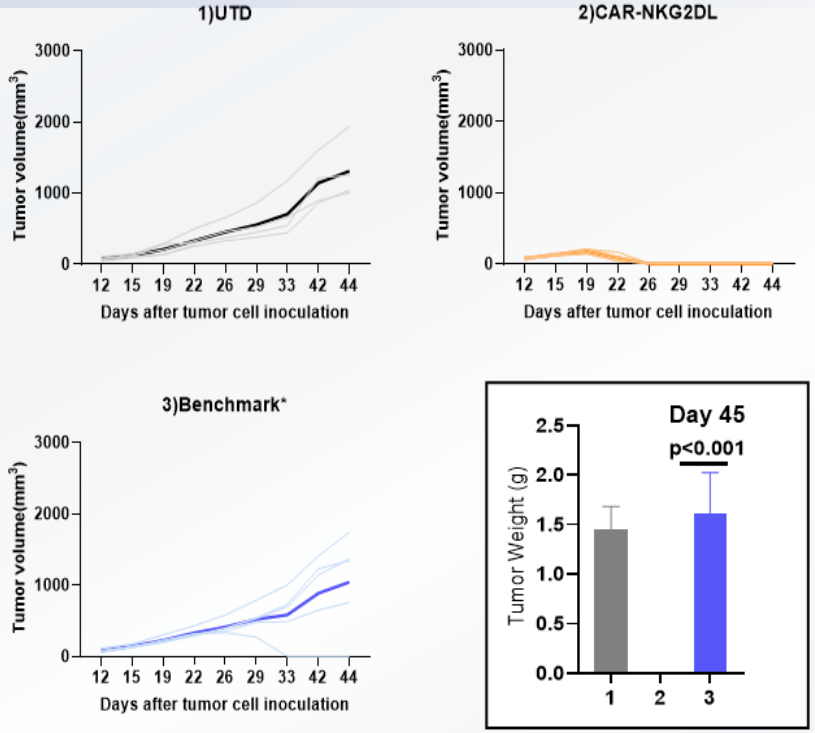
1. Shi Y, et al. *Cancer Commun* (Lond). 2023 Jul 21

Next-Gen CAR-T Development: Tackling Key Challenges in Solid Tumors

Next-gen Claudin18.2 CAR-T shows enhanced anti-tumor activity in GC models



Next-gen NKG2D CAR-T shows robust anti-tumor activity in HCC models



CT041-derived Armored CAR-T demonstrates enhanced therapeutic efficacy

Proprietary CAR-NKG2DL T cells achieve 100% clearance in HCC

Allogeneic CAR-T Platforms and Pipeline Products

CARSGEN THERAPEUTICS

Existing Efficacy Gap between Allogeneic CAR-T and Autologous CAR-T

Treatment and outcomes	Allogeneic BCMA CAR-T			Autologous BCMA CAR-T
	ALLO-715	P-BCMA-ALLO1[2]		cilta-cel
	3.2 x10^8 cells, N=24[1]	All Arm**: 0.25-6 x10^6 cells/kg, N=72	Arm C**:2 x10^6 cells/kg N=23	0.5-1 x10^6 cells/kg, N=97[3]
Enrolled	48	72	23 (including 2 retreatment)	113
Days to treatment initiation*	5	1	1	32
Required bridging therapy	0%	0%	0%	75%
ORR (mITT)	71%	54%	91%	98%
CR/sCR rate (mITT)	25%	11%	22%	80%
≥VGPR rate (mITT)	71%	33%	48%	95%
mDoR	8.3 months	7.7 months***	Not reported	Not reached****

*For ALLO-715, time is calculated from enrollment to lymphodepletion; for P-BCMA-ALLO1, time is calculated from enrollment to the start of study treatment.
**Four arms in total, Arm C (cy 750 mg/m^2/day +Flu 30 mg/m^2/day) P-BCMA-ALLO1 Dose 2 × 10^6 and Arm B (cy 1000 mg/m^2/day +Flu 30 mg/m^2/day) P-BCMA-ALLO1 Dose 2 × 10^6 , Arm S (cy 300 mg/m^2/day +Flu 30 mg/m^2/day) P-BCMA-ALLO1 Dose Range of 0.25-6×10^6, and Arm A (cy 500 mg/m^2/day +Flu 30 mg/m^2/day) P-BCMA-ALLO1 Dose 2 × 10^6 .
***The median duration of response (DoR) was 232 days for study Arms A and B – the cohorts with six or more months of follow-up at the time of data cut-off.
****Based on a median duration of follow-up of 18 months, mDOR=21.8 months.

1. Allogene Therapeutics. 2021. *ASH 2021 Presentation*. Accessed Nov 5, 2024
2. Poseida website news releases of phase 1 early results; Poseida Therapeutics. 2024. International Myeloma Society (IMS) 21st Annual Meeting and Exposition
3. ciltacabtagene autoleucel [Prescribing Information]. Janssen Biotech

Relatively Limited Expansion of Allogeneic CAR-T in Patients

- In allogeneic CAR-T, donor T cells will be recognized and rapidly eliminated by the host immune system (HvGR), which impacts CAR-T cell survival and results in limited expansion.
- Compared to autologous CAR-T, in vivo persistence of allogeneic CAR-T is significantly reduced.

Autologous and Allogeneic BCMA CAR-T in Multiple Myeloma

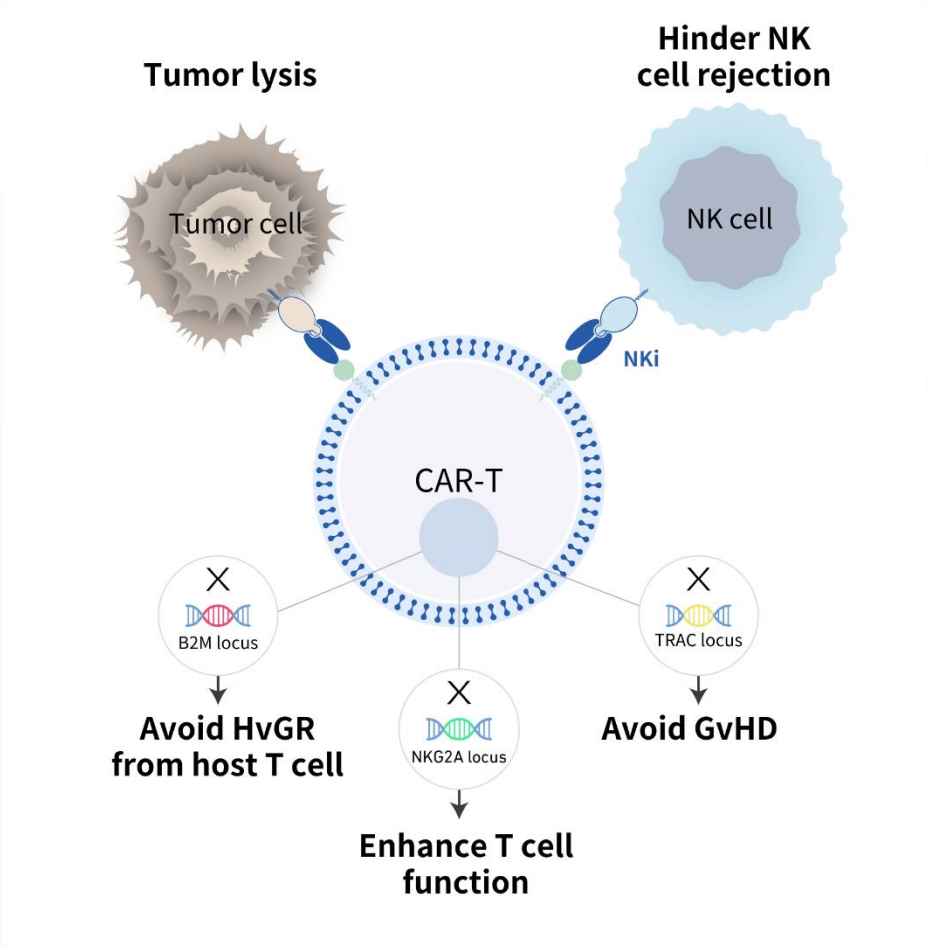
	Allogeneic CAR-T	Autologous CAR-T	
	ALLO-715	cilta-cel	zevor-cel
	UNIVERSAL Phase I[1]*	CARTITUDE-1[2]	LUMMICAR-1 Phase 1[3]
Median C_{max} (copies/ug gDNA)	**6,419***	**47,806**	**202,543**
Lymphodepletion Regimen	• Fludarabine: 30 mg m^2*3 days; • Cyclophosphamide: 300 mg m^2*3days; • ALLO-647 mAb**: 13mg/20mg/30mg*3days	• Fludarabine: 30 mg m^2*3 days; • Cyclophosphamide: 300 mg m^2*3 days;	• Fludarabine: 25 mg m^2*3 days; • Cyclophosphamide: 300 mg m^2*3 days

*Data from all patients (N=24) receiving the FCA regimen with 3.2 x10^8 cells.
**ALLO-647: A humanized anti-CD52 monoclonal antibody for the depletion of CD52-positive host lymphocytes.

1. Mailankody, S et al. *Nat Med* 29, 422–429 (2023)
2. ciltacabtagene autoleucel [Prescribing Information]. Janssen Biotech
3. W Chen, et al. *EHA 2024*. 2024 May

THANK-uCAR® or THANK-u Plus™: Innovative Allogeneic CAR-T Platform Aimed to Address Immune Rejection

Target and Hinder the Attack of NK cells on Universal CAR-T cells (THANK-uCAR®)



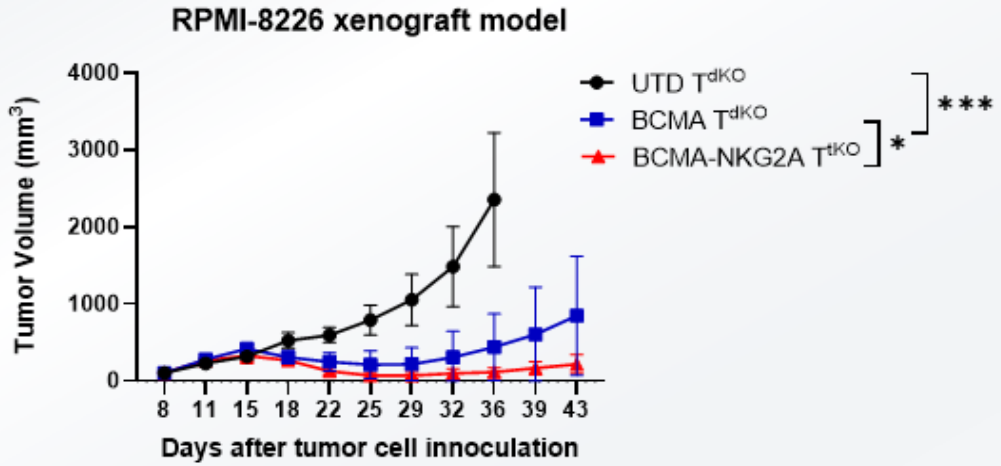
HvGR is the major challenge faced by Allogeneic CAR-T

- B2M knockout to overcome HvGR from host T cells, but NK cells attack uCAR-T cells without B2M.

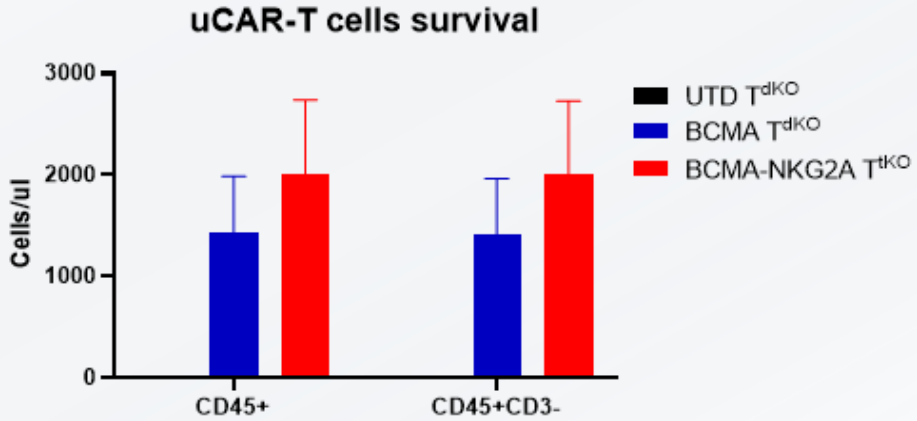
THANK-uCAR® to better address HvGR

- Anti-NKG2A CAR protects the uCAR-T cells from NK cell lysis.
- NK cells could act as “feeder cells” for uCAR-T cells, thereby enhancing the expansion of uCAR-T cells.
- NKG2A knockout can further enhance T cell functionality.

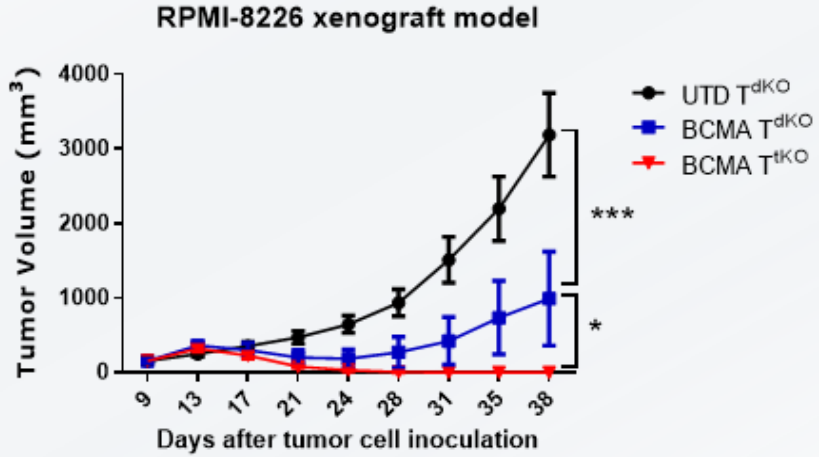
Enhanced in Vivo Antitumor Activity of NKG2A-Knocked-Out Allogeneic CAR-T Cells in the Absence of NK Cells



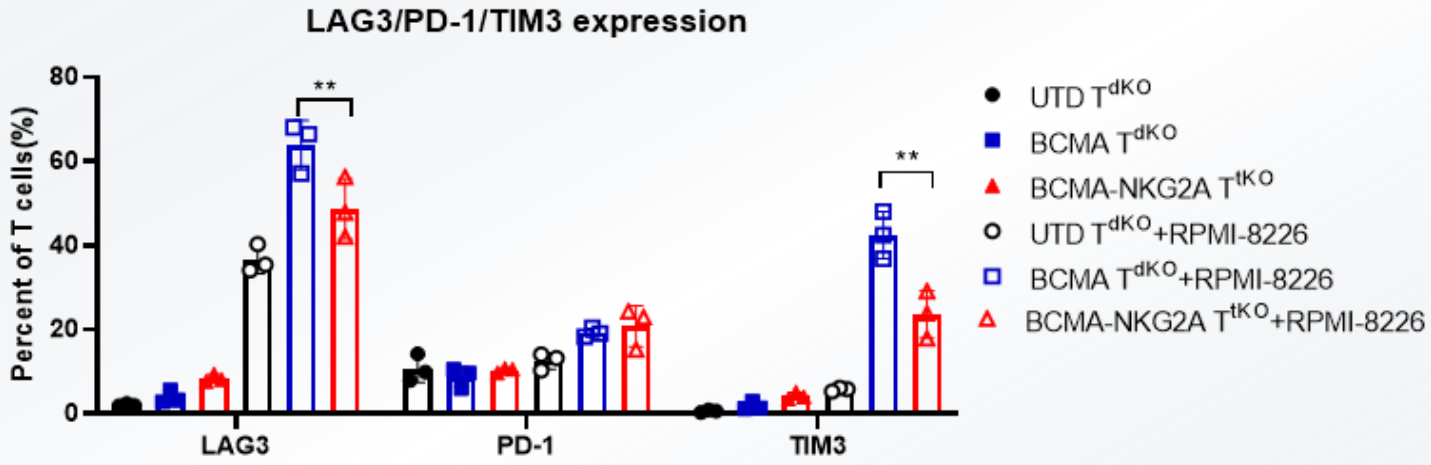
NKG2A/BCMA triple knock-out: improved efficacy



NKG2A/BCMA triple knock-out allogeneic CAR-T: enhanced in vivo persistence

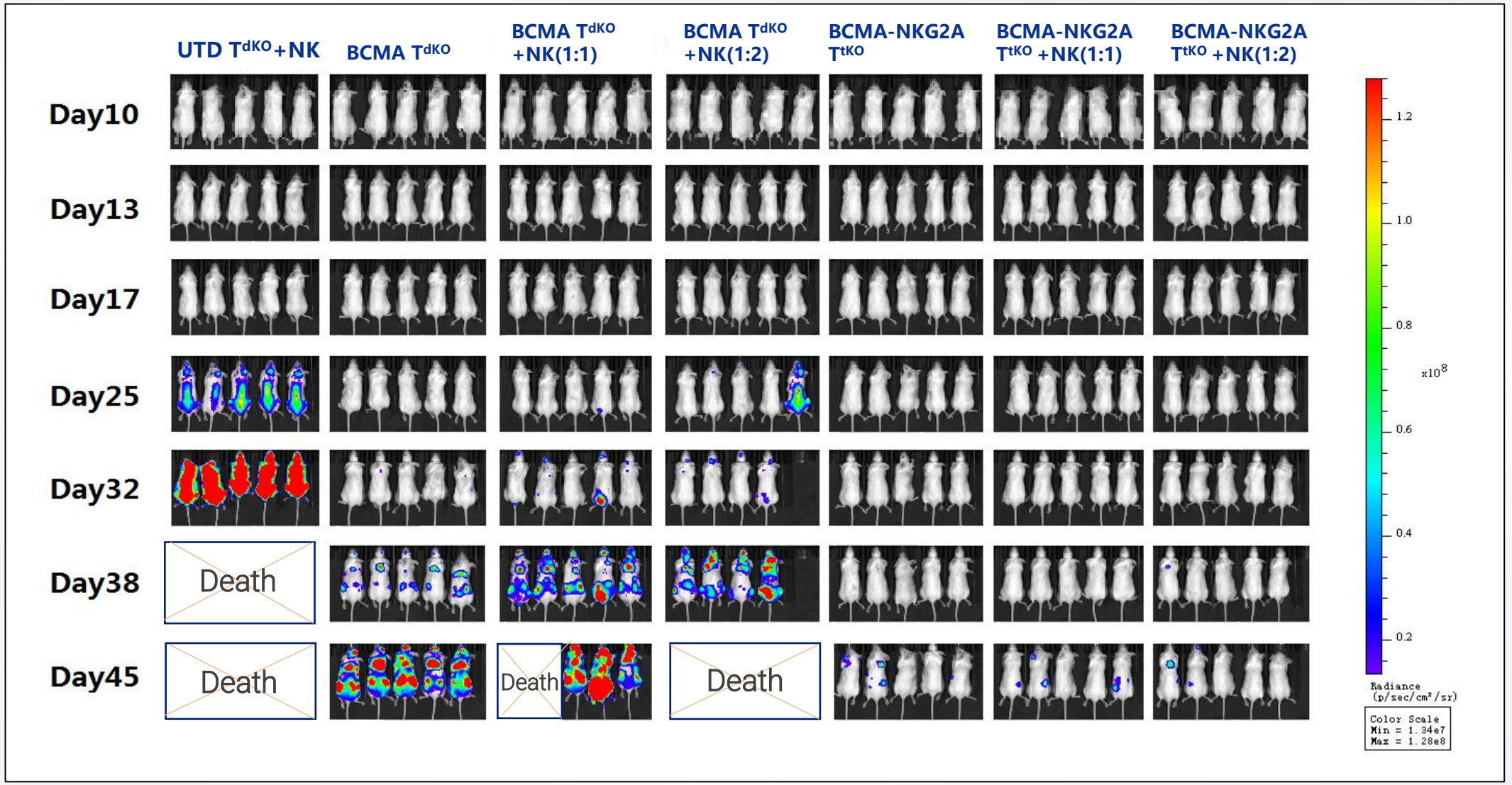


BCMA triple knock-out: improved efficacy



NKG2A/BCMA triple knock-out allogeneic CAR-T: lower expression

CT0590 Exhibits Enhanced in Vivo Antitumor Activity in Mice in the Presence of NK Cells



CT0590 IIT: Study Design

An open-label, single-arm, phase 1, first-in-human trial in China (NCT05066022).

Key eligibility

- 18-75 years
- Relapsed/Refractory multiple myeloma (RRMM) ≥ 3 prior regimens including at least one proteasome inhibitor (PI) and on immunomodulatory agent (IMiD) OR
- stable disease, relapse or progression following treatment with at least one PI or one IMiD; relapse within 12 months after the most recent therapy OR
- failed to achieve at least Minimal Response OR
- had progression within 60 days after most recent therapy
- ECOG 0-1

Primary endpoint

- Safety and tolerability

Secondary endpoints

- Pharmacokinetics
- Preliminary efficacy

Preconditioning

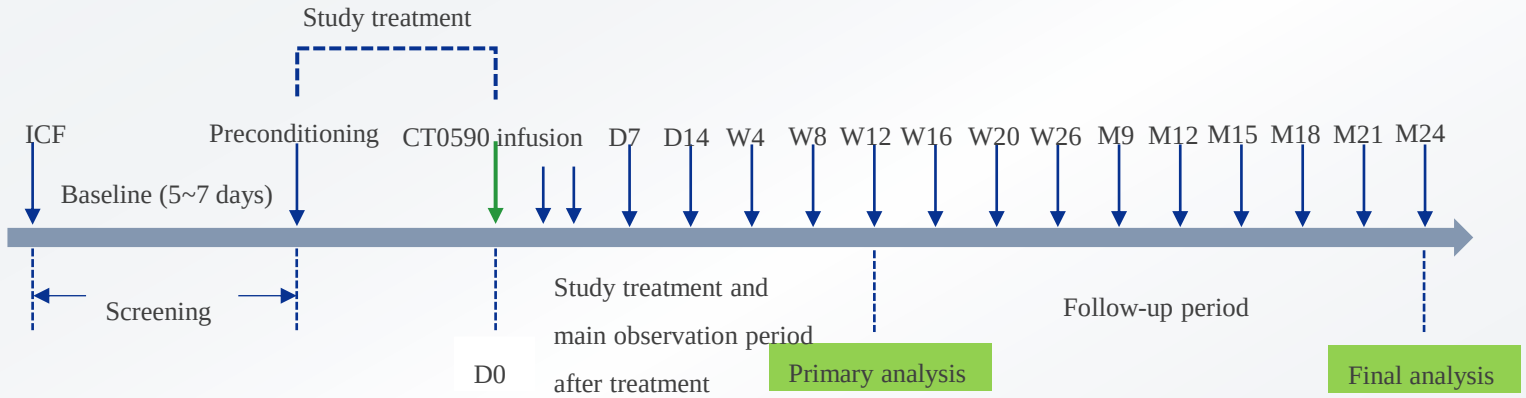
F: Fludarabine (30mg/m^2/day x 3days)

C: Cyclophosphamide (500 mg/m^2/day x 3 days)

i3+3 design; Doses:

50×10^6, 150×10^6, 300×10^6, 450×10^6 CT0590 cells

Subjects can be re-infused



1. Fu C, et al. 2024 ASH. 2024 Dec; Poster 4843

CT0590 IIT: Baseline Characteristics and Outcomes

Patient (Diagnosis)	High risk cytogenetics Y/N	ISS stage	# of prior lines	Refractoriness to PI/ IMiD*	% Baseline NKG2A expression NK cells	Best overall response	DOR (mo)	TTR (mo)	Peak CAR copy number (copies/µg gDNA)
PT 1 (MM)	Y	I	2	1	23	SD	NA	NA	BLQ
PT 1-reinf (MM)									5,102
PT 2 (MM)	Y	I	2	2	38	sCR	23	1.1	482,749
PT 3 (MM)	Y	III	3	2	12	SD	NA	NA	BLQ
PT 4 (MM)	Y	III	3	2	NA	PR	4	2.3	BLQ
PT 4-reinf (MM)						PR	6.9	2.4	
#PT 5 (pPCL)	N	NA	3	2	46	sCR	20	1.2	280,863

This patient was treated under compassionate use

Data cut-off : 22-Apr-2024

* 2 indicates double class refractoriness (to a PI and an IMiD), 1 indicates PT 1 patient refractory to a PI.

- As of April 22, 2024, a total of five patients have been enrolled, 80% of whom exhibited high-risk cytogenetics. Two patients had more than 60% plasma cells in their bone marrow. Both achieved sCR with a **DoR of ≥20 months** and CAR copy numbers of ≥200,000.
- In the subgroup analysis of the CARTITUDE-1 trial for the autologous BCMA CAR-T cilta-cel, patients with high-risk cytogenetics had an mDoR of **20.1 months**, while those with ≥60% plasma cells had an mDoR of **23.1 months**.

1. Fu C, et al. 2024 ASH. 2024 Dec; Poster 4843

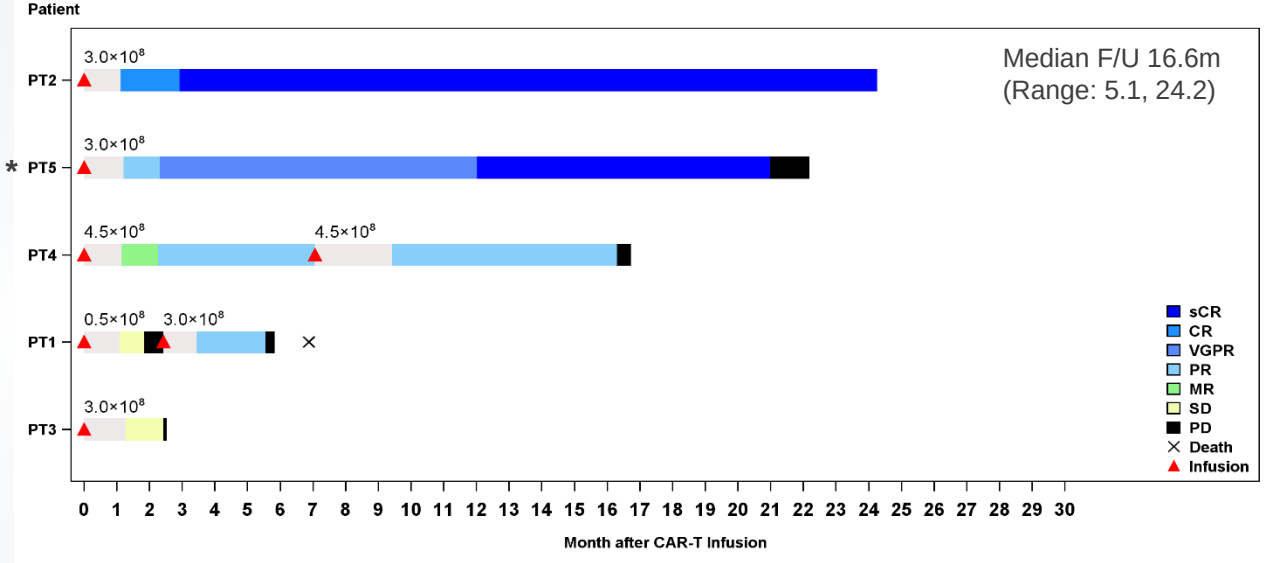
CT0590: Manageable Safety Profile

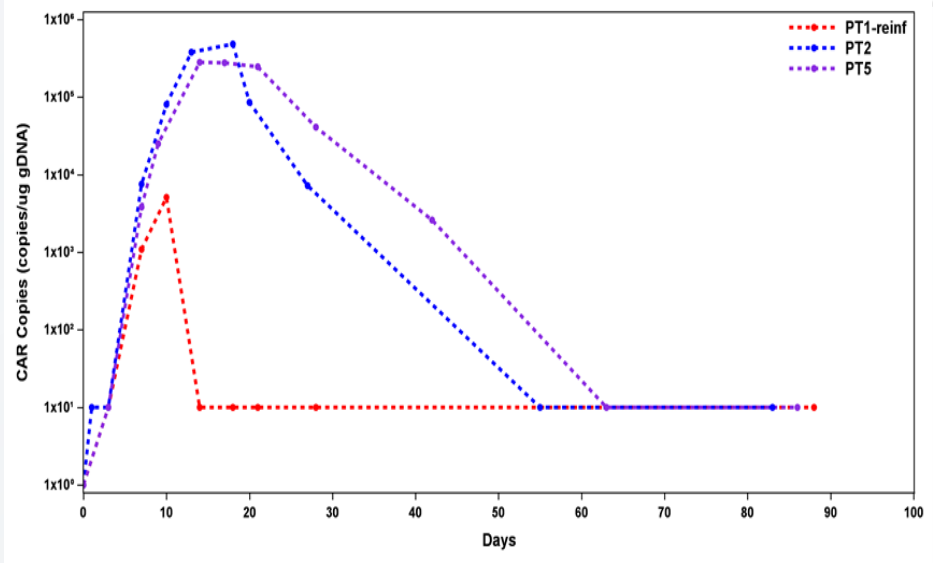
	n (%)
SAEs	1 (20.0)
Treatment related TEAEs	4 (80.0)
SAE	0
CRS	2 (40.0)
ICANS	0
GvHD	0
AEs leading to withdrawal	0
AEs leading to death	0
DLT	0

- Two patients experienced CRS
  - ✓ One patient each at Grade 1 and Grade 2; no ≥ Grade 3 CRS;
  - ✓ Time to onset was 8-10 days post-infusion;
  - ✓ Duration was 3-4 days.
- **No** cases of ICANS or GvHD were observed.
- **No** DLTs, **no** withdrawals due to AE, **no** deaths due to AE

1. Fu C, et al. 2024 ASH. 2024 Dec; Poster 4843

CT0590: Deep and Durable Responses





- 3 subjects achieved confirmed responses including **2** subjects with stringent complete response (sCR) and 1 subject with partial response (PR). Patient 1 achieved PR but it could not be confirmed due to COVID-19.

- CAR copies could be detected in 3 out of the 5 patients:
  - ✓ Patient 2 remained in remission at the time of data cut-off (Duration of Response [DOR]> 23months) ; achieved substantial peaks CAR copy numbers of **482,749 copies/μg gDNA** at 19 days;
  - ✓ Patient 5 with pPCL achieved sCR and was in remission for 20months; achieved substantial peaks CAR copy numbers of **280,863 copies/μg gDNA** at 15 days;
  - ✓ Both Patients with sCR presented with ≥ 80% bone marrow plasma cells at baseline;
  - ✓ No CAR copies were detected in any subject after Week 8.

1. Fu C, et al. 2024 ASH. 2024 Dec; Poster 4843

* Patient 5 with pPCL was treated under compassionate use

A Case of CT0590 to Treat R/R MM

Baseline Characteristics

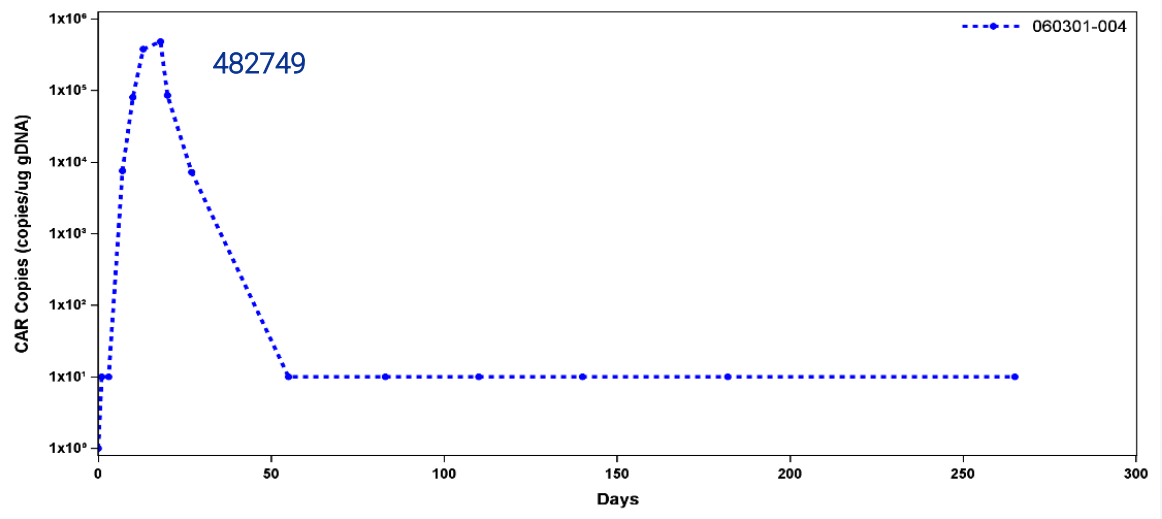
- A 71-year-old male diagnosed with MM,
- Double-refractory, with 94.5% plasma cells in bone marrow.
- 2 prior lines of therapies, including 3 regimens.
- Received 3×10^8 CT0590 CAR-T cells infusion.

Safety

- 1 Grade CRS
- Only 1 subject had Grade 3 treatment-related infection (pneumonia) on Day 12, which fully resolved.
- No ICANS

Efficacy

- W12: achieved sCR，with a DoR of ≥23 months (ongoing)



1. Fu C, et al. 2024 ASH. 2024 Dec; Poster 4843

A Case of CT0590 to Treat R/R pPCL

Baseline Characteristics

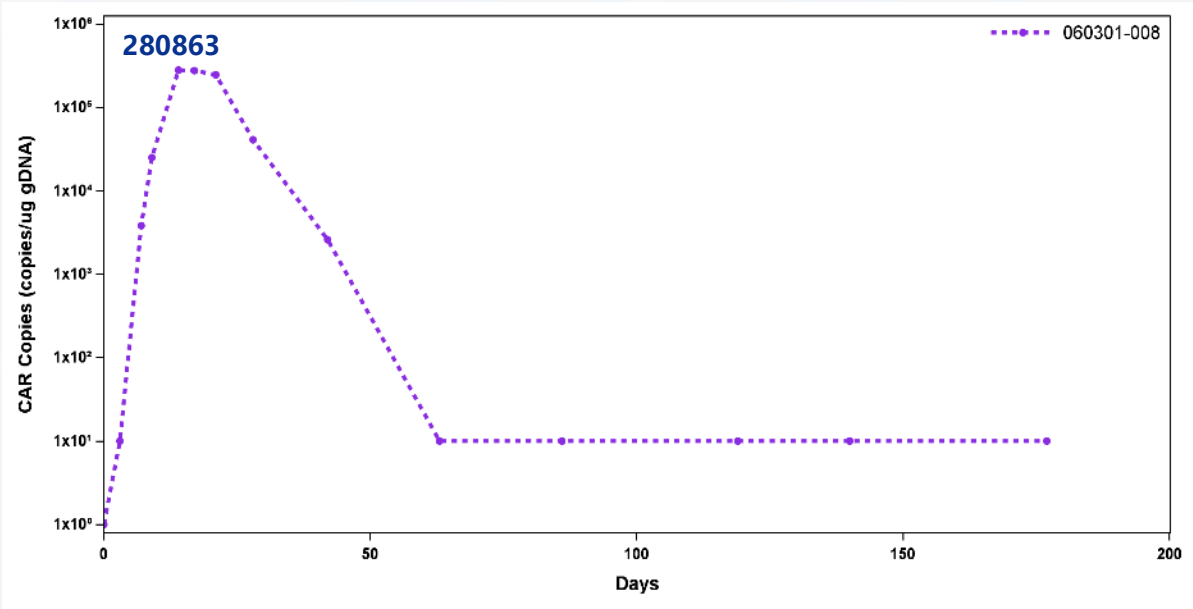
- A 52-year-old male diagnosed with pPCL
- Double-refractory
- 3 prior lines, including 3 regimens (ASCT, etc.)
- Received an infusion of 3×10^8 CT0590 CAR-T cells.

Safety

- 1 Grade CRS
- Grade 1 infection (pneumonia), unrelated to treatment.
- No ICANS

Efficacy

- sCR with a DoR of 20 months.
- The DoR is more than double the duration reported for autologous BCMA CAR-T treatments in PCL.



Best response	Duration of response	References
1 VGPR	117days (PFS)	Li, C, et al. Clin Transl Med. 2021;11(3):e346.
1 CR	307 days (PFS)	Li, C, et al. Clin Transl Med. 2021;11(3):e346.
1 sCR	7months (DoR)	Deng J, et al. Front Oncol. 2022; 12: 901266.

Previous reports of autologous BCMA CAR-T therapy for multiple myeloma show that the DoR is less than 10 months.

1. Fu C, et al. 2024 ASH. 2024 Dec; Poster 4843

Baseline NKG2A Expression on NK cells may be Predictive of CT0590 Responses

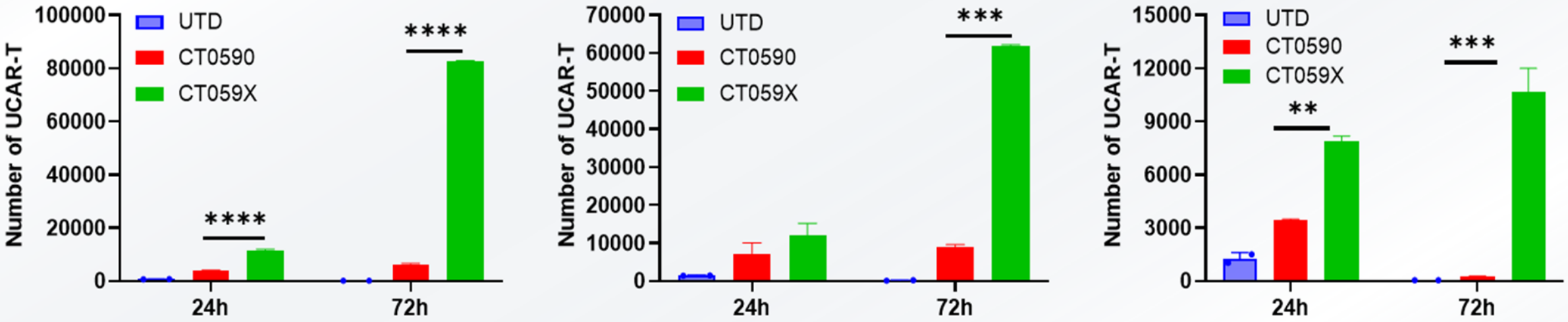
- 4 patients had baseline NKG2A data available.
- Both patients who attained sCR, Patient 2 and Patient 5, had relatively higher NKG2A expression levels on NK cells at 38% and 46% respectively.
- A relatively weak expansion of CT0590 CAR-T cells in vitro in the presence of NK cells with lower NKG2A expression was observed (data not shown here).
- Baseline NKG2A expression levels on NK cells may predict treatment outcomes with CT0590.

Patient (Diagnosis)	Dose (cells)	% Baseline NKG2A expression NK cells	Best overall response
PT 1 (MM)	50×10^6	23	SD
PT 1-reinf (MM)	300×10^6		
PT 2 (MM)	300×10^6	**38**	**sCR**
PT 3 (MM)	300×10^6	12	SD
PT 4 (MM)	450×10^6	NA	PR
PT 4-reinf (MM)	450×10^6		PR
PT 5 (pPCL)	300×10^6	**46**	**sCR**

1. Fu C, et al. 2024 ASH. 2024 Dec; Poster 4843

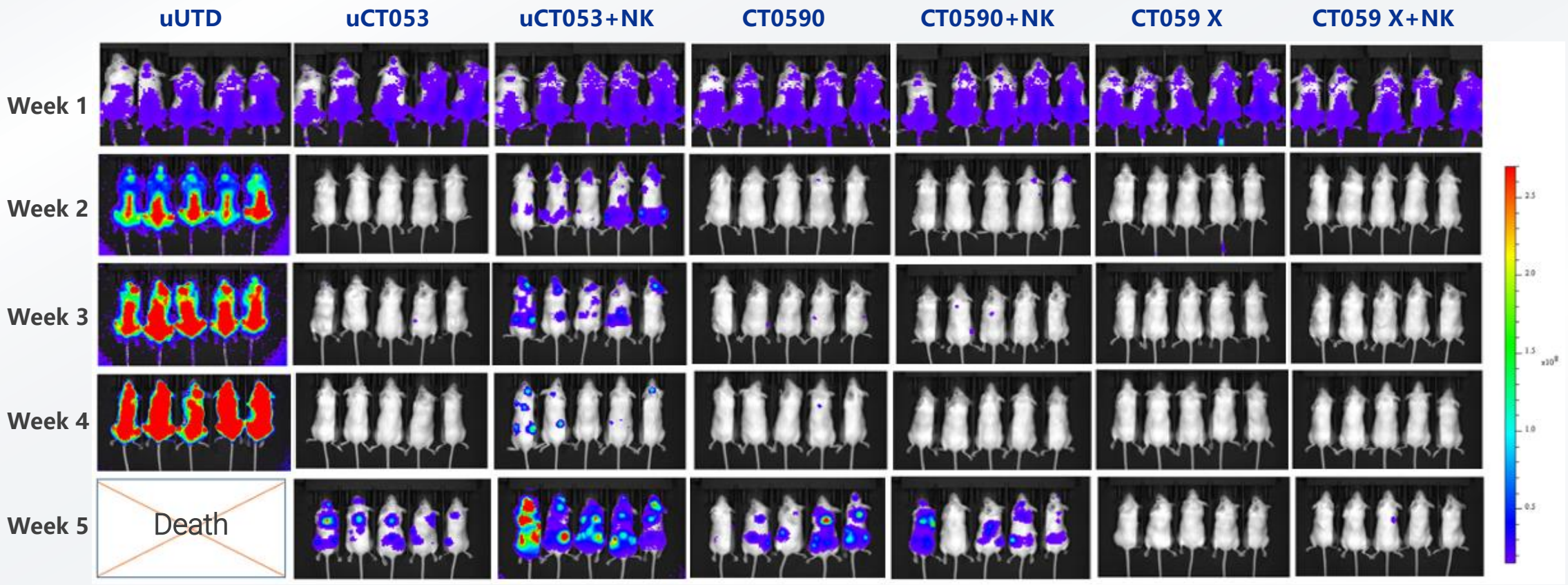
THANK-u Plus™: Enhanced and Sustained Allogeneic CAR-T Expansion Across Different NKG2A Expression Levels

NKG2A expression: **High** **Medium** **Low**



- THANK-uCAR CT0590 exhibits a decrease in expansion within 72 hours in NK cells with relatively low NKG2A expression, while the expansion of CT059X, produced using THANK-u Plus™, continues to increase over time.
- CT059X expanded significantly better than CT0590 in the presence of NK cells with medium or high levels of NKG2A expression.

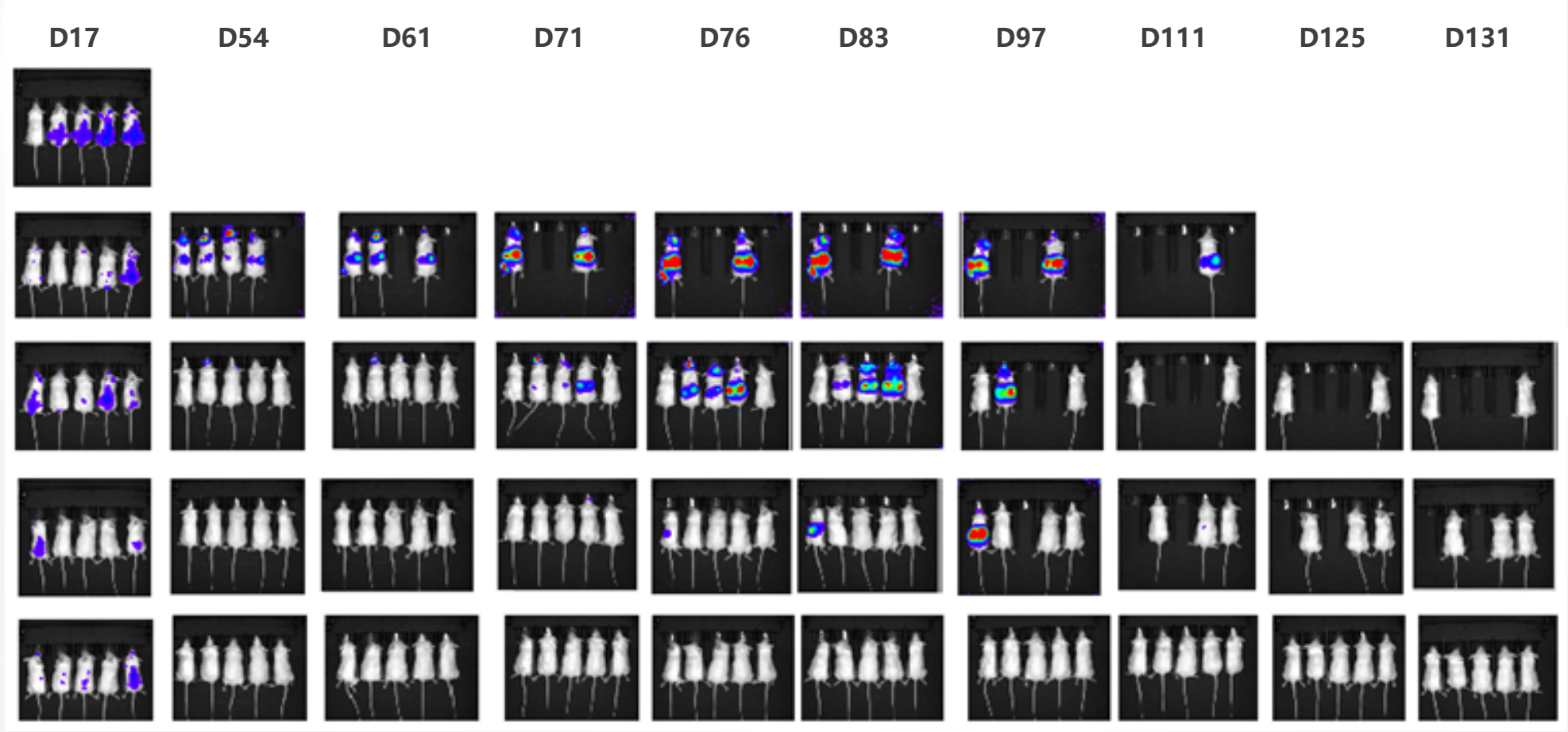
THANK-u Plus™ Demonstrates Enhanced Anti-Tumor Efficacy in vivo



CT059 X demonstrates significantly greater efficacy than allogeneic CT053 and CT0590, in the presence or absence of NK cells.

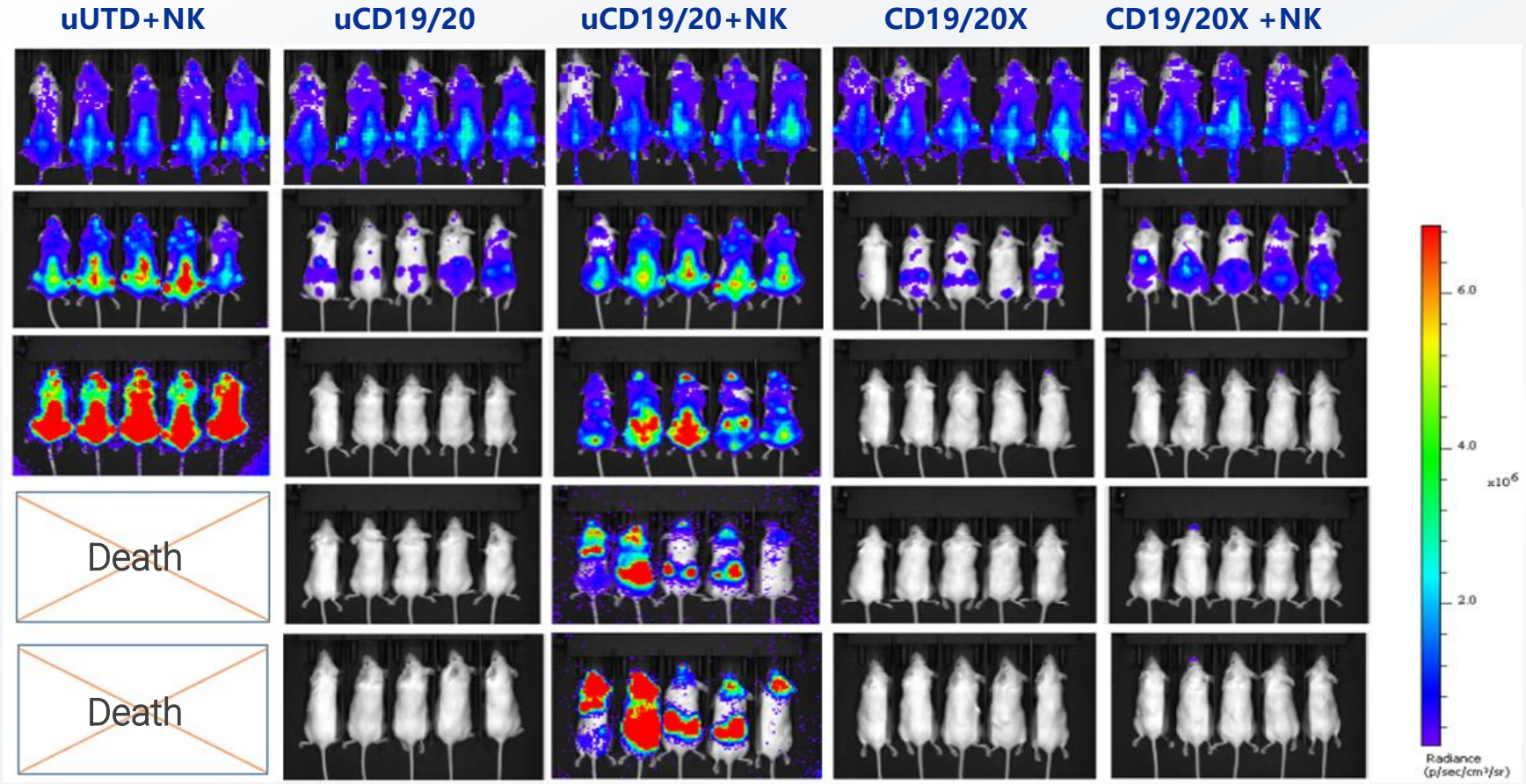
Note: uUTD refers to untransduced allogeneic T cells.

Proprietary Allogeneic CD19/CD20 CAR-T Demonstrates Potential Best-in-class Efficacy in Lymphoma Models



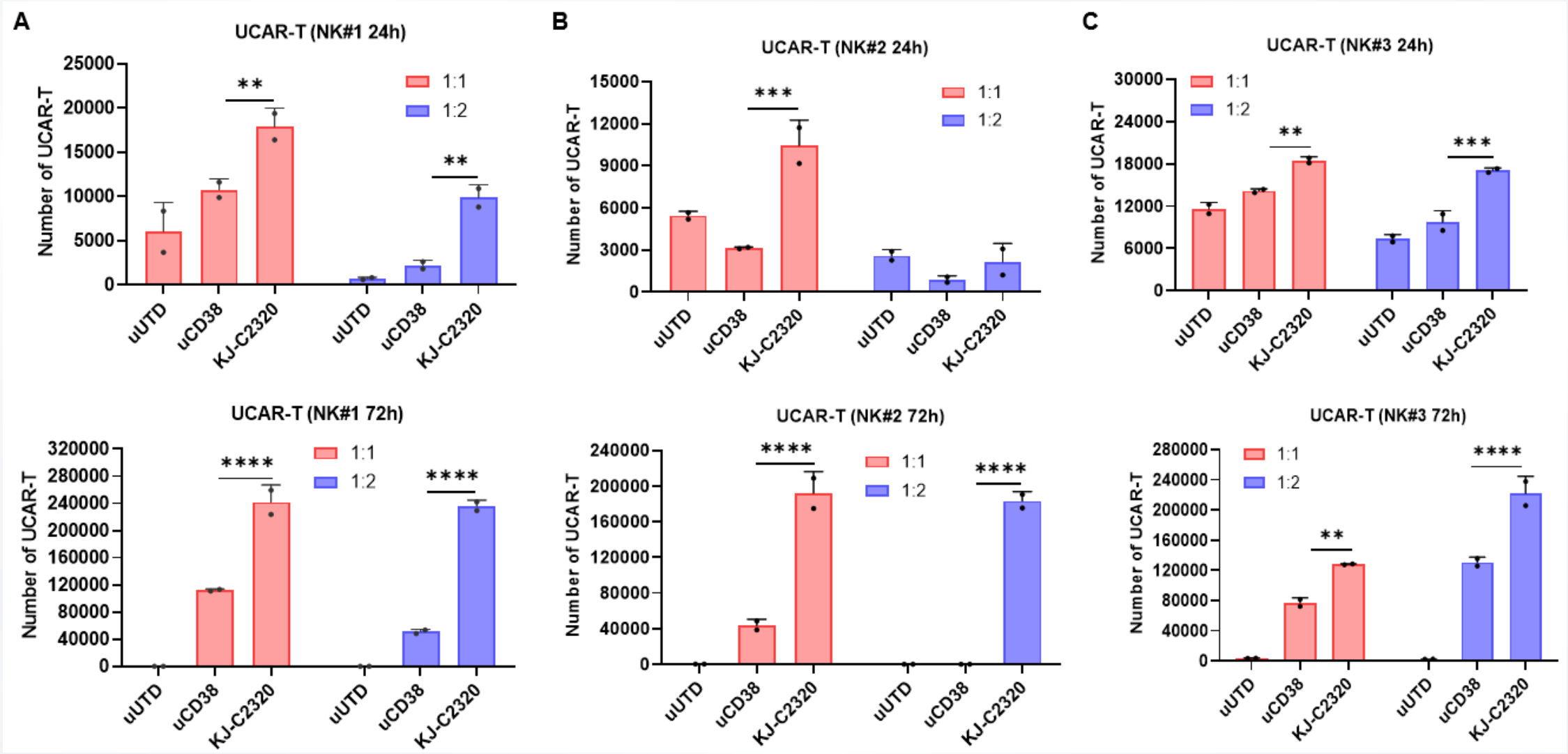
CARsgen's allogeneic CD19/CD20 dual-target CAR-T demonstrates superior efficacy in a B-cell lymphoma model, over CD19 or CD20 single-target CAR-Ts, and benchmark CD19/CD20 dual-target CAR-T.

CD19/20X Allogeneic CAR-T Exhibits Robust Anti-lymphoma Activity in the Presence of NK Cells

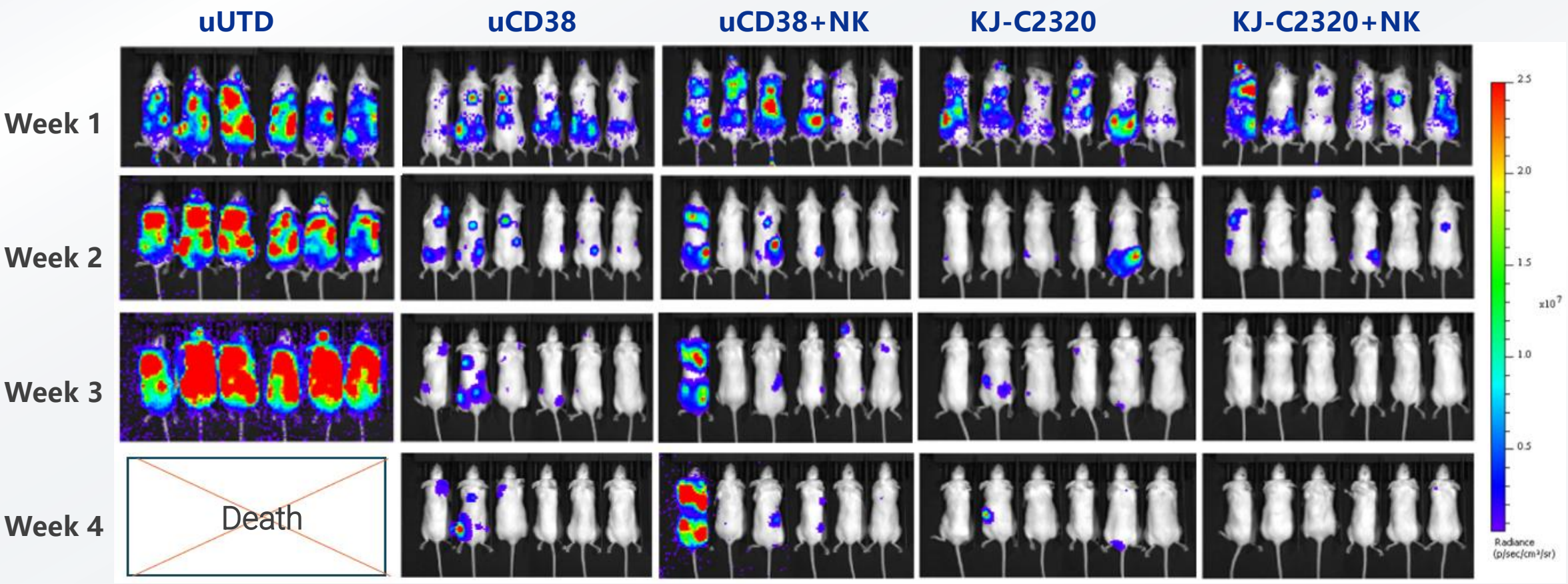


In the presence of NK cells, CD19/20X allogeneic CAR-T (THANK-u Plus™ platform) demonstrates much better anti-tumor efficacy than conventional allogeneic CD19/20 CAR-T.

The Sustained and Enhanced Expansion of KJ-C2320 in the Presence of NK Cells from Different Donor Sources



KJ-C2320 Exhibits Enhanced Antitumor Activity in Mice in the Presence of NK Cells



Summary of CARsgen's Allogeneic CAR-T Platform

- The allogeneic CAR-T therapies targeting BCMA, CD19/CD20, and CD38 currently under development have demonstrated potent anti-tumor efficacy in mouse models, particularly in the presence of NK cells.
- Several allogeneic CAR-T products are currently in development:
  - CT0590 – targeting BCMA, for R/R MM and R/R PCL (enrollment finished).
  - CT059X – targeting BCMA, for R/R MM and R/R PCL, an IIT initiated. The first subject has achieved sCR, following infusion of CAR-T cells at the lowest dose level according to the clinical protocol.
  - KJ-C2219 – targeting CD19/CD20, for B-cell malignancies, an IIT initiated; for systemic lupus erythematosus and systemic sclerosis, an IIT initiated.
  - KJ-C2320 – targeting CD38, for AML, an IIT initiated.
  - KJ-C2114 – for solid tumors.
  - KJ-C2526 – targeting NKG2DL, for AML, other malignancies, senescence.
- On February 25, 2025, CARsgen Therapeutics introduced Zhuhai SB Xinchuang to accelerate allogeneic CAR-T cell products development in mainland China.

Multiple Value Inflection Milestones in the Near Future

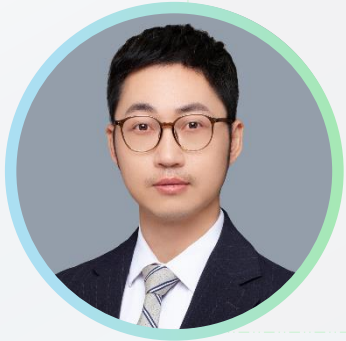
- **H1 2025**: Planned NDA submission for CT041 to the NMPA.
- **2025 ASCO**: Expected disclosure of CT041 China Phase II pivotal trial data in 3L gastric cancer.
- **H2 2025**: Anticipated data release for CT041 in pancreatic cancer adjuvant therapy.
- Multiple allogeneic CAR-T products are advancing through development, with upcoming data updates:
  - CT059X for R/R MM and R/R PCL;
  - KJ-C2219 for B-cell malignancies and autoimmune diseases;
  - KJ-C2320 for AML;
  - KJ-C2114 for solid tumors;
  - KJ-C2526 for AML, other malignancies, and senescence.

Experienced Senior Management Team

Zonghai Li, MD, PhD
Co-founder, Chairman of the Board, CEO, CSO

Huamao Wang, PhD
Co-founder and COO

Hua Jiang, MD, PhD
Vice President, Early Discovery



Yi Luo, MD, PhD
Vice President, Clinical Sciences

Nishan Rajakumaraswamy, MD
Vice President, US Clinical Sciences Head

Andy (Peng) Zang, PhD
Vice President, Head of Business Development and Strategic Planning

Making Cancer Curable

CARSGEN
THERAPEUTICS