CARSGEN THERAPEUTICS

CARsgen Therapeutics (HKEX: 02171)

December 2023

Making Cancer Curable

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Highlights of Developments and Milestones in the First Half of 2023

Clinical and Regulatory Development

- Phase 2 clinical trial for CT041 in the U.S. has been initiated.
- IND clearance achieved for adjuvant treatment of pancreatic cancer for CT041 in China
- Data update on AB011 Phase 1 clinical trial at 2023 ASCO GI
- Initiated IIT for CT071 (Fully-human GPRC5D CAR-T)

Business Development

- Agreement with Huadong Medicine (SZ. 000963) for the commercialization of zevor-cel in mainland China.
- Agreement with Moderna, INC. (Nasdaq. MRNA) to evaluate CT041 in combination with an mRNA cancer vaccine

Manufacture Efficiency optimization

- The CGMP Manufacture Facility located in North Carolina, USA is now under full operation, overall manufacturing operational efficiency improved.

Financial Highlight

- By June 30 of 2023, the cash and Cash equivalents is about Rmb2.174 billion and expected cash runway into 2026.

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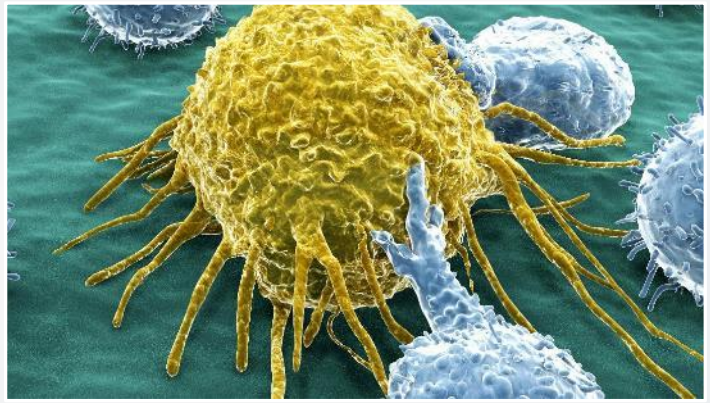
CAR T Cells: Initial Successes in B-cell Malignancies Unlocked a Journey of Significant Opportunities and Challenges



CAR T cells: ultimate solution to “cure” cancer

T cells: **pivotal** role in immune system

Rapid **expansion**

Flexibility in **engineering**

Clinically **proven**

Initial successes in B-cell malignancies

- Revolutionary efficacy and product approval in treatment of **B-cell malignancies.**
- Lack of breakthrough beyond B-cell malignancies

Challenges with CAR T, particularly for solid tumors

- Lack of ideal **target**
- Tumor **heterogeneity**
- Hostile tumor **microenvironment**

What it takes to develop effective CAR T-cell therapies

- **Insight**
- **Infrastructure** in R&D and manufacturing
- Operational **efficiency**

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Since 2014, CARsgen Has Been a Pioneer in CAR T-cell Research and Development

Research

Discovery and innovation

Cancer Types
- GBM, HCC, GC, PAAD, etc.

Targets
- First-in-class GPC3 CAR T (CT011)
- First-in-class CLDN18.2 CAR T (CT041)

Combinations
- e.g. CAR T + TKI

Lympho-depletion
- e.g. FNC regimen (FC + Nab-Paclitaxel)

Development

Antibodies

In-house antibody development platforms
- Phage display
- Hybridoma

Humanized/fully-human antibodies developed against **~20 targets**

CAR T technologies

A suite of proprietary technologies
- For both **autologous** and **allogeneic CAR T cells**
- For both **hematological malignancies** and **solid tumors**

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Experienced Senior Management Team in China & US

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

Huamao Wang, PhD
Co-founder and COO

Raffaele Baffa, MD, PhD
Chief Medical Officer

Leigh Hsu, PhD, MBA
Senior Vice President, Business Development

Sylvie Peltier, PharmD, MHL
Senior Vice President
Global Regulatory Affairs

Hong Ma, MD, MS, MBA
Senior Vice President
Clinical Sciences

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CARsgen's Competitive Product Pipeline with Global Rights

	Product Candidate[1]	Technology	Target	Indication	Pre-clinical / Phase I / Phase II/III[2] / BLA NDA
CAR T-cell therapies	**Zevor-cel (CT053)[3]**	Conventional	BCMA	R/R MM	LUMMICAR 1 (China)
				R/R MM	LUMMICAR 2 (US, Canada)
				R/R MM	IIT (China)
	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)
	CT011		GPC3	HCC	(China)
	CT0180	sFv-ε	GPC3	HCC	IIT (China)
	CT0181		GPC3	HCC	IIT (China)
	CT0590	THANK-uCAR®	BCMA	R/R MM	IIT (China)
	CT048	CycloCAR®	Claudin18.2	GC/GEJ and PC	IIT (China)
	CT071	CARcelerate™	GPRC5D	R/R MM, R/R pPCL	(US)
				R/R MM, R/R pPCL	IIT (China)
	KJ-C2113	CycloCAR®	Mesothelin	Solid tumors	
	KJ-C2114	THANK-uCAR®	Undisclosed	Solid tumors	
	KJ-C2320	Undisclosed	Undisclosed	AML	
mAb	**AB011**		Claudin18.2	GC/GEJ and PC	Mono & Combo (AB011+CAPOX) (China)

[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)

for hematologic malignancies for solid tumors

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; AML: acute myeloid leukemia

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Zevor-cel (CT053): a Potential Best-in-class BCMA CAR T

Zevor-cel Highlights

- ✓ Optimized scFv with enhanced binding affinity and stability
- ✓ Competitive efficacies
- ✓ Excellent safety
- ✓ Fast-to-market
  - NDA accepted by China NMPA (Oct 2022);
  - Phase 2 trial in North America: Ongoing
- ✓ Designations: RMAT (FDA), PRIME (EMA), Orphan Drug (FDA & EMA); Breakthrough Therapy Drug (NMPA)

38 heavily pretreated R/R MM patients (IIT + China Phase 1)[1]

- **High Disease Burden**

Extramedullary disease	High-risk cytogenetics
31.6%	50%

- **Competitive Efficacy and Safety Profile**

ORR	sCR/CR	mPFS	mDOR
92.1%	78.9%	22.7 mos	24.0 mos

Treatment-related death	≥Grade 3 CRS	≥Grade 3 Neurotoxicity*
0%	0%	2.6%

*epilepsy (fully resolved after methylprednisolone treatment)

1. Chengcheng Fu, et al. ASH 2021. Abstract 1751.

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CT041: First-in-class CLDN18.2 CAR T with Breakthrough Efficacy Data[1]

CT041 Highlights

- ✓ First-in-class CLDN18.2 CAR T
- ✓ Optimized scFv with enhanced binding affinity and stability[2]
- ✓ Optimized preconditioning
  - (FC + low-dose Nab-Paclitaxel)
- ✓ Globally first solid tumor CAR T in pivotal trial
  - GC (3L+) Confirmatory Phase II trial in China: Ongoing
  - GC (3L+) Phase 2 trial in North America: Ongoing
  - PC Adjuvant Therapy Phase I trial in China: Ongoing
- ✓ Designations: RMAT (FDA), PRIME (EMA), Orphan Drug (FDA & EMA)

nature medicine ARTICLES
https://doi.org/10.1038/s41591-022-01800-8
Check for updates

OPEN

Claudin18.2-specific CAR T cells in gastrointestinal cancers: phase 1 trial interim results

18 GC/GEJ patients who had failed at least 2 prior lines of therapies at a dose 2.5×10^8 CAR T cells.

ORR	DCR	DOR rate at 6 months
61.1%	83.3%	57.1%

mPFS*	mOS*
5.6 mos	9.5 mos

*PFS and OS above were calculated from CAR T infusion date.

SOC in GC/GEJ patients who had failed at least 2 prior lines of therapies

Lonsurf (trifluridine/tipiracil) TAGS[3]			Opdivo (Nivolumab) ATTRACTION-2[4]		
ORR	mPFS	mOS	ORR	mPFS	mOS
4.5%	2.0 mos	5.7 mos	11.2%	1.6 mos	5.3 mos

1. Qi C, et. al. *Nat Med.* 2022 Jun;28(6):1189-1198
2. Jiang H, et al. *J Natl Cancer Inst.* 2019;111(4):409-418
3. Shitara K, et. al. *The Lancet Oncol.* 2018;19(11):1437-1448
4. Kang, Yoon-Koo et al. *The Lancet.* 2017;390(10111):2461-2471

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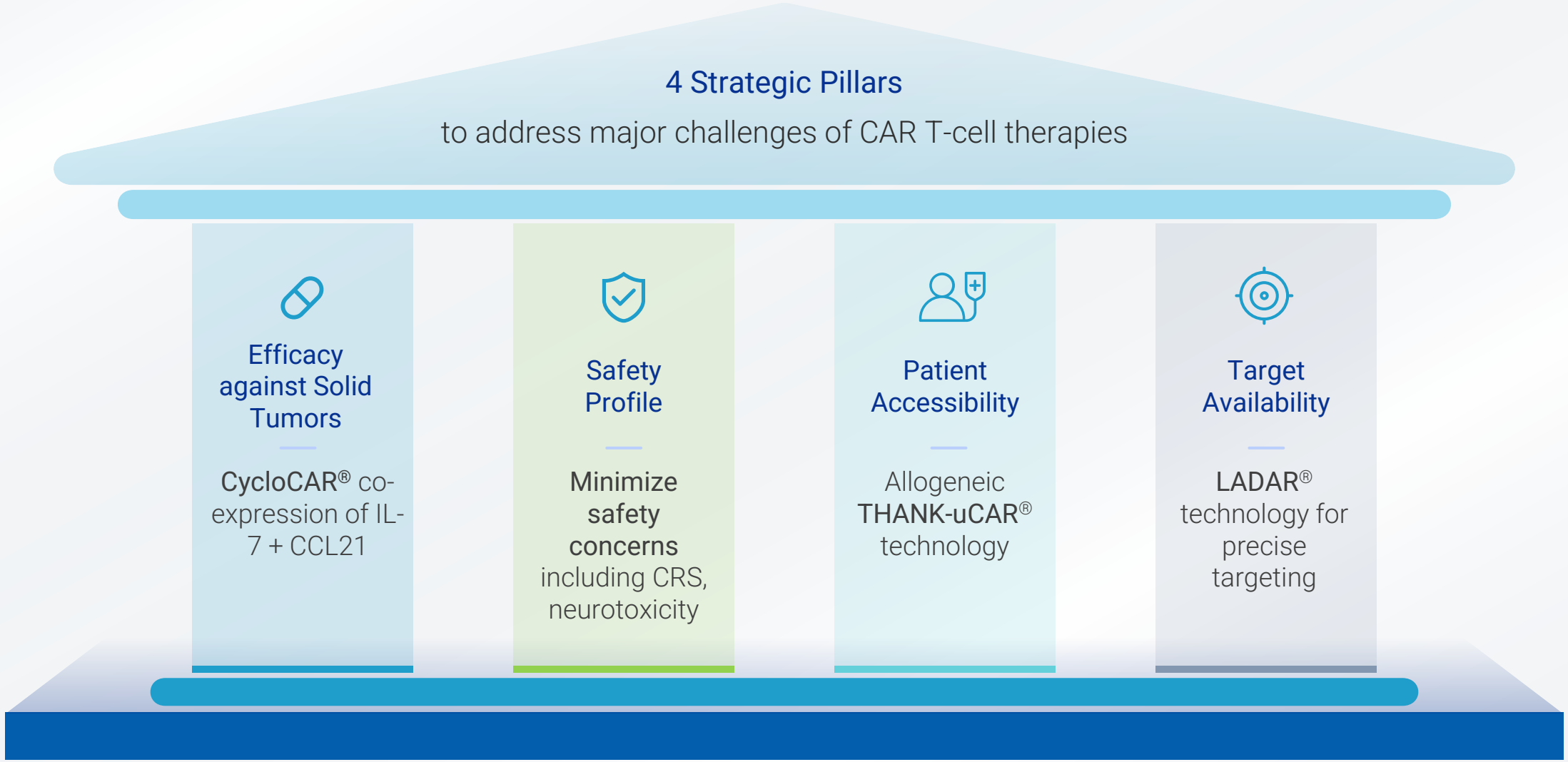
A Suite of Technology Platforms to Empower the Development of Next-Generation CAR T-cell Products



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

Shanghai
Headquarters, research, clinical development, two GMP manufacturing facilities

Durham, North Carolina
CGMP manufacturing facility

Houston, Texas
Clinical development

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 CT041 in combination with an mRNA Cancer Vaccine

inno.N
(KOSDAQ: 195940)
License of zevor-cel and CT032 in the Republic of Korea

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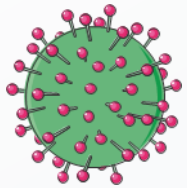
Integrated Internal Capabilities to Maximize Development Speed, Robust Clinical/Commercial Supply, and Competitive Cost

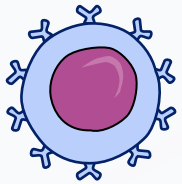
Plasmid

Clinical grade Plasmid DNA up to multiple-gram per batch



Lentiviral vectors

One batch of lentiviral vectors can support **hundreds of** batches of CAR T cells



CAR T cells

- Manufacturing success rate **>95%**
- Clinical grade CAR T cells up to $3x10^{10}$ cells/lot

Central lab

GLP, GCP compliant platforms covering

- Method development and validation
- Clinical sample test (PK/PD, immunogenicity, new biomarkers)

Companion Diagnostics

CDx development and registration

- CLDN18.2
- GPC3
- New Biomarkers

Bioprocess Analysis

Regulatory compliant well-characterized assays

- Kits development and manufacturing
- Cell/Molecular/Immunology assays

Nucleic acid and protein manufacturing

GMP grade nucleic acid and protein manufacturing for both clinical and commercialization

- Nuclease
- Guide RNAs
- Recombinant proteins & antibodies

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Harnessing Manufacturing Capabilities in China and the U.S. for Maximized Synergies and Flexibilities

Xuhui, Shanghai

—

~200 CAR T batches annually

Jinshan, Shanghai

—

~2000 CAR T batches annually

Raleigh-Durham, North Carolina

—

~700 CAR T batches annually

"In China for global markets"

Lentiviral vectors

- CARsgen Shanghai Facility has been the manufacturer of lentiviral vectors for clinical trials the U.S.

CAR T cells

- Exploring using CARsgen shanghai facility to supply CAR T cells for global market

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CARsgen's Strategic Development Roadmap

Establish
Extend
Explore

Establish

- Approval and Commercial launch
  - ✓ Zevor-cel (BCMA)
  - ✓ CT041 (CLDN18.2)

(Fast-to-market)

Extend

- Earlier lines of therapies
  - ✓ CT041 (CLDN18.2)
  - ✓ CT011 (GPC3 for HCC)
- New Targets
  - ✓ CT071 (GPRC5D)

(Maximize the value)

Explore

- New cancer types
  - ✓ KJ-C2320 (AML)
- Combination
- New technology
- Allogeneic

(Explore the uncharted)

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Multiple Value Inflection Milestones in the Future

Zevor-cel (BCMA CAR T)	• Expected to obtain NDA approved from NMPA at the end of 2023 or the beginning of 2024 • Expected to complete enrollment in the Phase 2 clinical trial in the US by the end of 2023 • Expected to submit a BLA to the FDA in the US in the first half of 2025
CT041 (CLDN18.2 CAR T)	• Expected to submit an NDA to the NMPA in China in 2024 • Expected to submit a BLA to the FDA in the US in 2025
New Products /New INDs	• Multiple INDs for earlier lines of therapies for existing products • Multiple new products: CT071 (GPRC5D) for MM, KJ-C2320 for AML, etc.

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Financial Highlights – Higher Adjusted Loss and Adequate Cash into 2026

Selected Consolidated Financial Information

	Six months ended June 30,	
(RMB'000)	**2023**	**2022**
Research and Development Expenses	-323,313	-316,304
Operating Losses	-409,230	-367,692
Loss for the year	**-404,472**	**-376,338**
Adjusted net loss*	**-385,726**	**-352,888**

	As at June 30, 2023	As at December 31, 2022
Cash, Cash equivalents and Terms deposits	**2,174,008**	**2,268,036**
Bank borrowings	**4,979**	**7,373**

2023 Guidance

Continue to strengthen R&D efforts

Estimate of full year 2023 financial performances:

Expected adjusted net loss and net loss at similar level as those in 2022.

Cash, equivalents and deposits at the end of 2023 are expected to be

≥ 1.6 billion RMB

Expected adequate cash into

2026

* Adjusted net loss represent the net loss excluding the effect of certain non-cash items and one-time events, namely the fair value loss of the financial instrument issued to investors, the listing fee and share-based compensation.

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Zevor-cel: Potential Best-in-class BCMA CAR T

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Multiple Myeloma: Significant Unmet Medical Needs

The 2nd most common hematologic malignancy

- An estimated ~560K patients worldwide will have MM by 2027

2022 Epidemiology

Incidence	~20K
Prevalence	~110K
First-line treatable cases	~30K
Second-line or later treatable cases	~40K

Incidence	~30K
Prevalence	~110K
First-line treatable cases	~30K
Second-line or later treatable cases	~25K

MM has a lower 5-year survival rate than other blood cancers (2000-2016 data)

5-year survival	Global[1]	US[2]	China[1]	Japan[1]
Lymphoma	40-70%	68%	38%	57%
MM	30-50%	50%	25%	33%

1. Allemani C, et. al. *The Lancet.* 2018 Mar 17;391(10125):1023-1075
2. Surveillance, Epidemiology, and End Results (SEER) Program; US, United States

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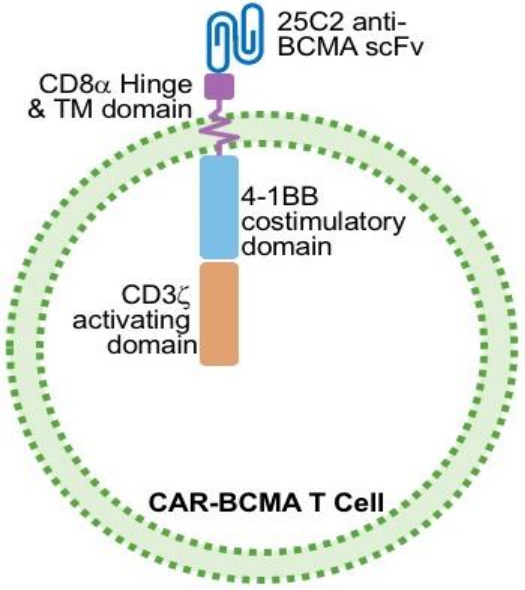
Zevor-cel (CT053): BCMA CAR T with Optimized scFv to Enhance Efficacy and Safety

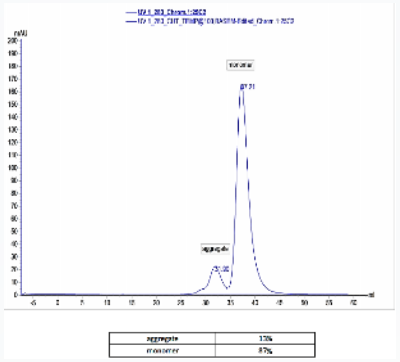
High Binding affinity (pM level)[1]

	KD(M)
BCMA	4.548E-10



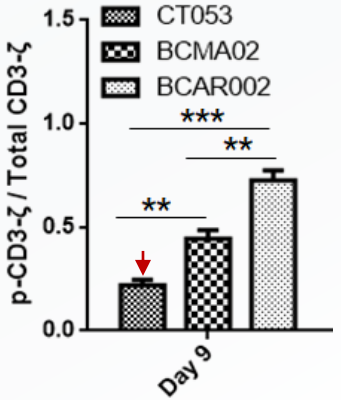
High stability

High Monomer Ratio (~90%)

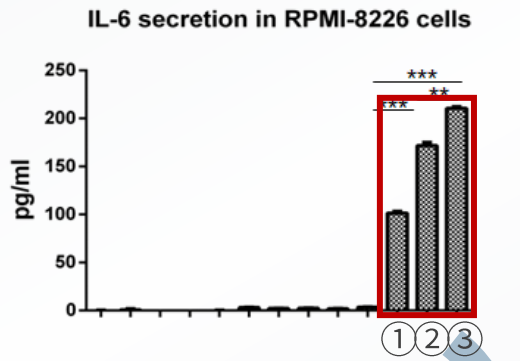


Reduced antigen-independent clustering

Less CD3 autophosphorylation than ABECMA® and CARVYKTI™



Less IL-6 expression than ABECMA® and CARVYKTI™



① CT053
② BCMA02 CAR
③ BCAR002 CAR

*BCMA02 CAR was made according to the construct ABECMA®
**BCAR002 CAR was made according to the construct of CARVYKTI™

1.Yang, Min et al. *Haematologica* vol. 107,8 1960-1965. 2022 Aug 1

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IIT and LUMMICAR-1 Efficacy and Safety Data

	China investigator-initiated trials[1]	China Phase I (LUMMICAR-1)[2]	China Phase II (LUMMICAR-1) [3]
Sample size	24	14	102 (60 with at least 12w follow-up for efficacy analysis)
EMD+	41.70%	14.30%	6.70%
High risk Cytogenetic	50%	50%	58.30%
Prior therapies	5 (2-11) regimens	6 (3-11) regimens	6 (3-17) regimens
ORR	87.50%	100%	91.70%
CR/sCR rate	79.20% (41.7% with ~6 M median follow up; 70.8% with ~9 M follow-up; 79.2% with ~15 M follow-up)	78.60%	56.70% (34/60, not mature)
≥VGPR rate	83.3% (20/24)	92.9% (13/14)	86.7%
Median follow-up	17.4 months	13.6 months	8.7 months
mDOR	21.8 months	12m-rate 100%	6m-rate 96.1%
mPFS	18.8 months	12m-rate 85.7%	6m-rate 91.2%
MRD negative	/	100% (11/11)	96.3% in patients with ≥VGPR
≥Grade 3 CRS	0	0	4.9%
≥Grade 3 NT	1/24 (4.2%)	0	0
Treatment related death	0	0	1

1. Yang M, et. al. *Haematologica*. 2022 Aug 1;107(8):1960-1965
2. Chen W, et. al. ASH 2021. 2021 Dec; Abstract #2821
3. Unpublished data, Efficacy based on IRC evaluation

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LUMMICAR-2 Phase 2: Preliminary Data Suggest Competitive Efficacy and Safety Profile in the US

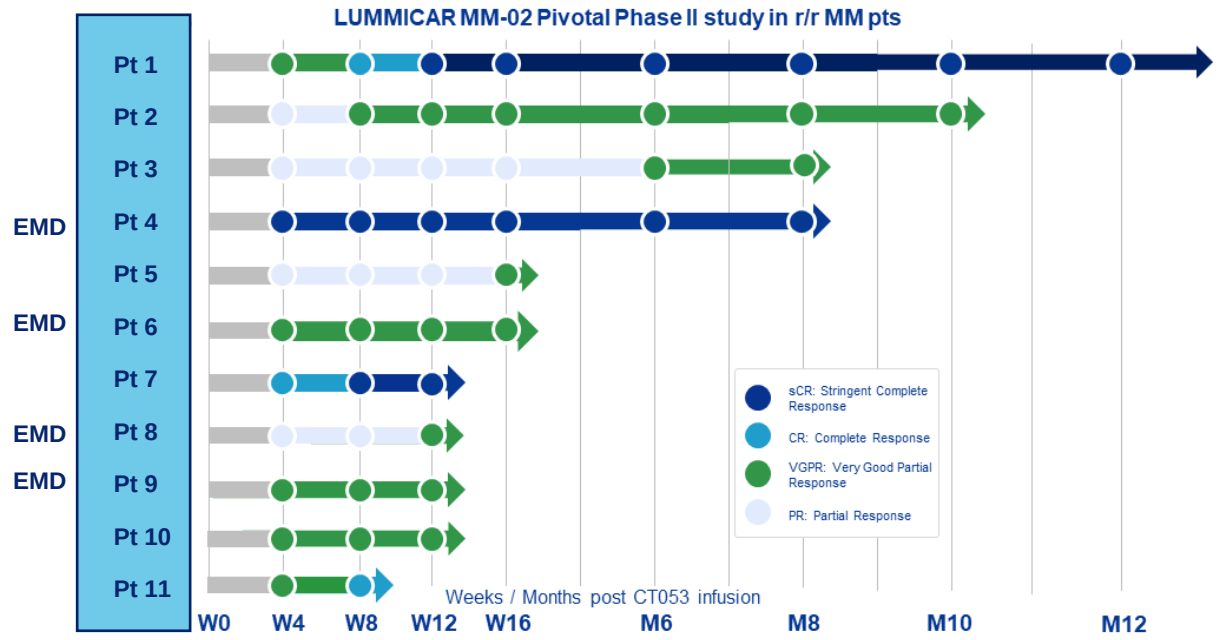
Competitive efficacy

- 100% responses at Week 4 (VGPR, CR or sCR) and ongoing
- Responses deepened with longer follow-up
- 100% MRD negative in all patients with available results at Week 4 by next-generation sequencing

Sample size	17 treated,11 evaluated
Patient Population	5/17(29.4%) EMD 9/17(52.9%) high risk
No. of prior therapies, median (range)	6 (4-17)
ORR	11/11 (100%)
CRS	10/17 (59%)
Grade 1 CRS	6/17 (35%)
Grade 2 CRS	4/17 (24%)
≥Grade 3 CRS	0
ICANS	3/17 (17.6%)
Grade 1 ICANS	2/17 (11.8%)
Grade 2 ICANS	0
Grade 3 ICANS	1/17 (5.9%)
Toxicity Mgmt: tocilizumab	5/17 (29%)
Toxicity Mgmt: corticosteroid	1/17 (5.9%)
Treatment related death	0

Best-in-class safety profile

- No treatment related death, no patient was admitted to ICU for CRS/ICANS
- No grade 3 or higher CRS (41% without any grade of CRS)
- 1/17 (5.9%) Grade 3 ICANS and fully resolved; No parkinsonism
- Minimal use of medication for toxicity mgmt (29% tocilizumab rate)
- 3 patients have received outpatient treatment



Data cutoff date: August 19, 2022

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Claudin18.2 Franchise Pipeline Products

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Addressing Large Population of CLDN18.2 Positive Tumors with Significant Unmet Medical Needs

According to *Global Cancer Statistics 2020*:

>1.5 million incident case for just gastric cancer and pancreatic cancer combined worldwide

	Gastric cancer	Pancreatic cancer
Incidence	1,089K	496K
Mortality	769K	466K

Gastric Cancer

5-year survival rate of advanced gastric cancer is 5-20%

3L+

ORR	mPFS	mOS
4.5%	< 2 mos	< 6 mos

Pancreatic Cancer

5-year survival rate ~6%

2L+

No effective SOC

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Claudin18.2 Franchise Offers a Comprehensive Multi-Modal Solution for Patients

CT041
First-in-class Claudin 18.2 CAR T

AB011
Globally second IND cleared Claudin 18.2 mAb (first humanized)

CT048
IL-7 and CCL-21 co-expression to enhance efficacy

CARsgen proprietary CLDN18.2 IHC test kit with high sensitivity and specificity

Gastric Cancer

(≥1+, any percentage)
77%

Pancreatic Cancer

(≥1+, any percentage)
66%

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CT041: Global First-in-Class CAR T for CLDN18.2-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)
- **PRIME** (EMA)
- **Orphan Drug** (EMA & FDA)

Collaboration

CARsgen and Moderna, Inc. (Nasdaq: MRNA) have initiated a collaboration agreement to investigate of CT041 in combination with Moderna's investigational Claudin18.2 mRNA cancer vaccine

Clinical Development Plan

- GC (3L+) Confirmatory Phase II trial in China: Ongoing
- PC Adjuvant Therapy Phase I trial in China: Ongoing
- Plan to submit the NDA in 2024

- GC (3L+) Phase 2 trial in North America: Ongoing
- Plan to submit the BLA in 2025

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

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CT041: Consistent Data Trend Reported in ASCO 2022 for Phase 1 trials in China and the US

	China investigator-initiated trials (NCT03874897)[1]	Phase Ib/II in China (NCT04581473)[2]	Phase 1b in the US (NCT04404595)[3]
Sample size	28 GC/GEJ 5 PC 4 other cancers	14 GC/GEJ	5 GC/GEJ 9 PC
ORR in GC/GEJ	**61.1%***	**57.1%**	**60%**
Median follow-up	7.6 m*	8.8 months	/
mPFS	**5.6 months***	**5.6 months**	**Not reached**
mDOR	6.4 months*	/	Not reached
mOS	9.5 months*	10.8 months	/
≥Grade 3 CRS	0	1**	0
≥Grade 3 ICANS	0	0	0
Treatment related death	0	0	0

*18 patients with GC/GEJ who had failed at least 2 prior lines of therapies at a dose 2.5×10^8 CAR T cells.
**One patient was related to the investigational disease and fully recovered after corticosteroids treatment.

1. Qi C, et. al. *Nat Med.* 2022 Jun;28(6):1189-1198
2. Qi C, et. al. ASCO 2022. 2022 Jun; Abstract #4017
3. Botta G, et. al. ASCO 2022. 2022 Jun; Abstract #2538

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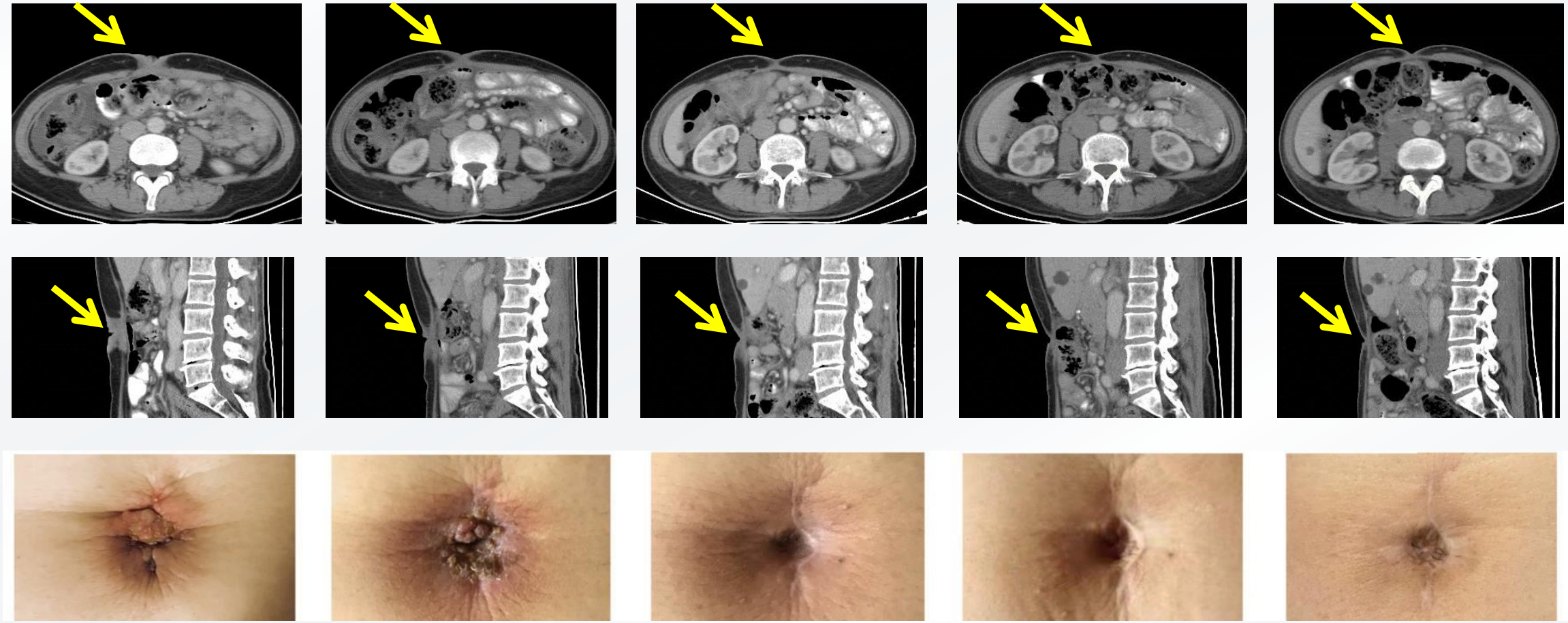
Case Sharing : Long-term Tumor Response

Pt08, 57/F, GC with peritoneal metastasis and Sister Mary Joseph nodule, had received 3 prior lines of therapy including PD-1 antibody, achieved PR and ongoing response more than 56 weeks, CLDN18.2 2+ 80%.



Pre-infusion | Post-infusion W4 | W12 | W24 | W40

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AB011: Globally First IND Approved Humanized CLDN18.2 mAb

Competitive Advantages

- The first CLDN18.2-targeted mAb developed in China that has received IND clearance from the NMPA
- Potentially more potent anti-tumor activity compared to current industry frontrunner

Clinical Trial and Plan

Excellent tolerability, safety and efficacy

Clinical Trial Overview	• Phase I dose-escalation and dose-expansion (mono therapy) enrollment completed • Phase I dose-escalation (AB011 + chemo) enrollment completed • Phase I dose expansion (AB011+chemo) enrollment completed
CLDN18.2 CDx	• CARsgen's proprietary CLDN18.2 IHC test kit being developed as CDx • High sensitivity and specificity

Source: Prospectus

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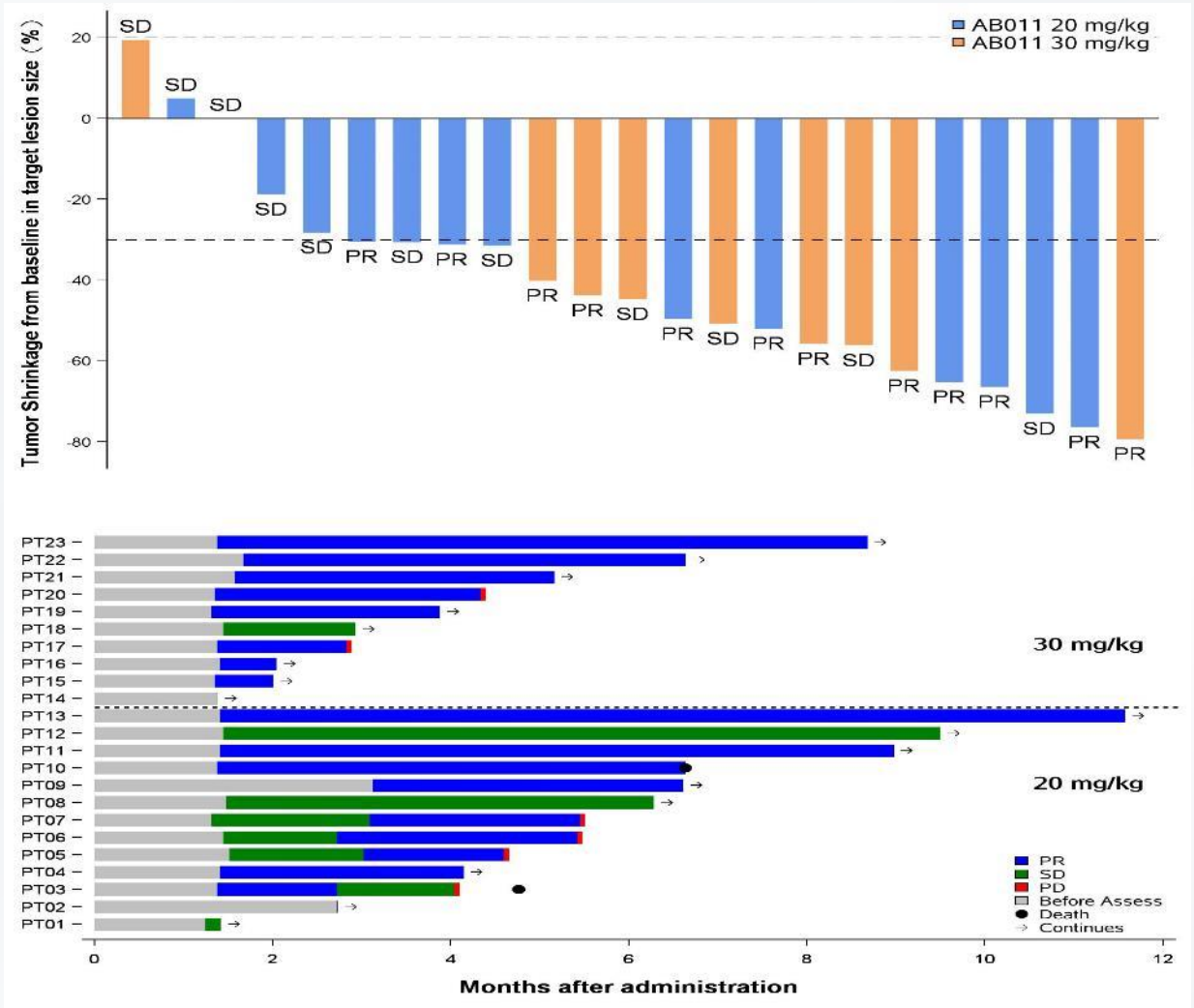
Compelling Efficacy of AB011+chemo Reported for 1L GC/GEJ in ASCO GI 2023

Completed Phase 1 Enrollment (NCT04400383)[1]

- AB011 monotherapy
- AB011 + CAPOX



ORR (RP2D)
53.8%
(not mature)

DCR
100%

1. Jin Li, et al. ASCO GI 2023 Abstract 391

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GPC3 Pipeline Products

CARSGEN THERAPEUTICS

Hepatocellular Carcinoma: The Third Leading Cause of Cancer Mortality Worldwide

2022 HCC Epidemiology in the US and China

Incidence	~40K
First-line treatable cases	~30K
Second-line or later treatable cases	~15K

Incidence	~600K
First-line treatable cases	~250K
Second-line or later treatable cases	~100K

HCC 5-year survival rate

	Global[1]	US[2]	China[3]
HCC, all stages	18%	20%	12%

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

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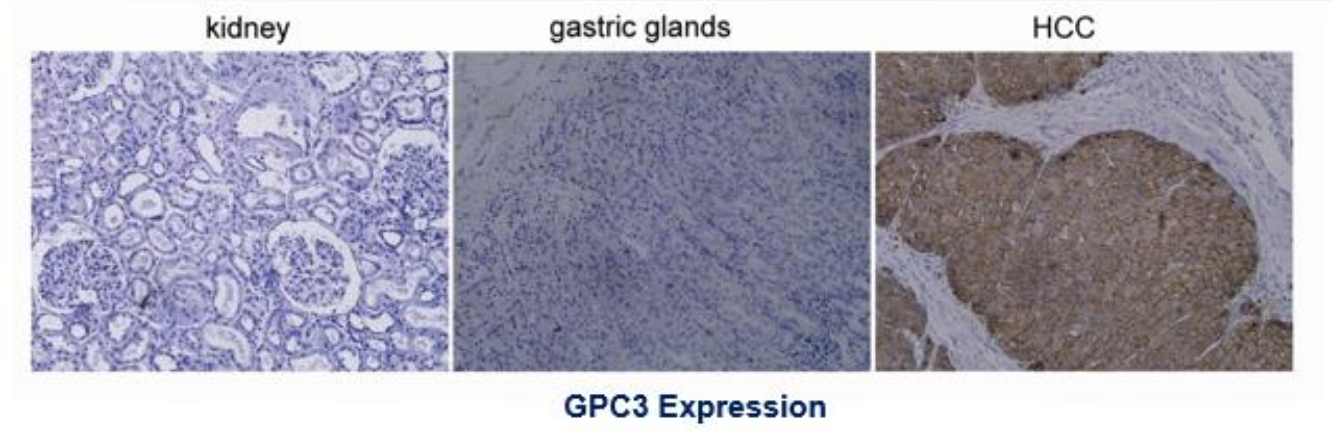
GPC3 is an Ideal Target for CAR T Cells to Treat HCC

GPC3: high expression and specificity

- GPC3 is a cell surface protein that belongs to the acetyl heparan sulfate proteoglycan family
- High expression in HCC and no expression in other 21 tested tissues, including heart, spleen, lung and kidney



GPC3 Expression

- GPC3 is also overexpressed in other cancer types

>60% of lung squamous cell carcinoma (SCC)

GPC3 Expression in HCC with CARsgen IHC test*

70.7%

Medium and High
54.6%

Low
16.1%

*CARsgen internal data

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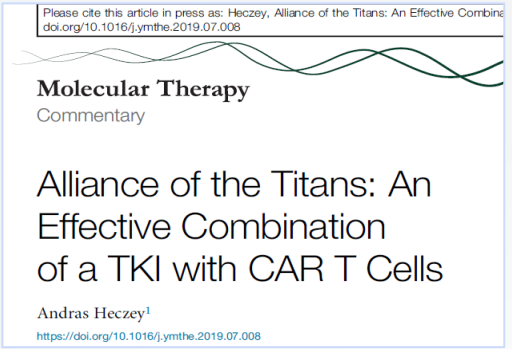
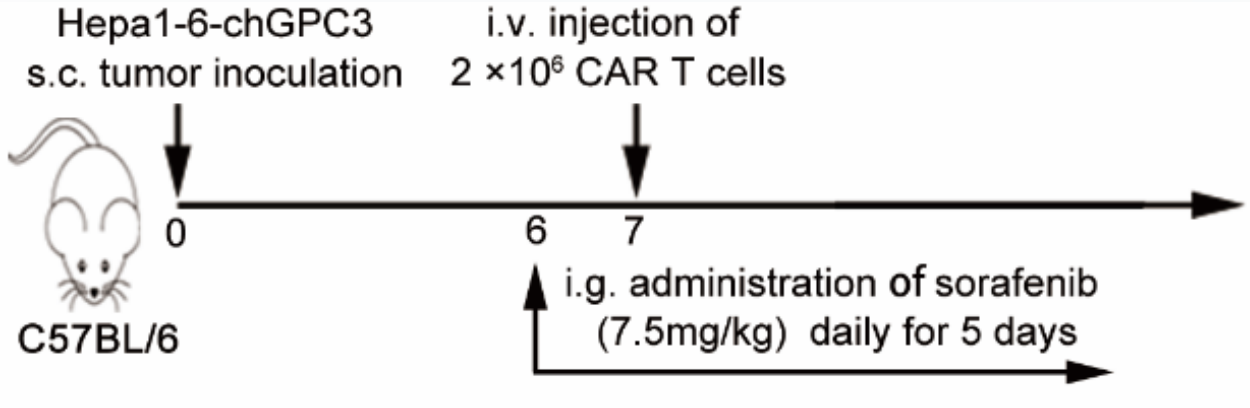
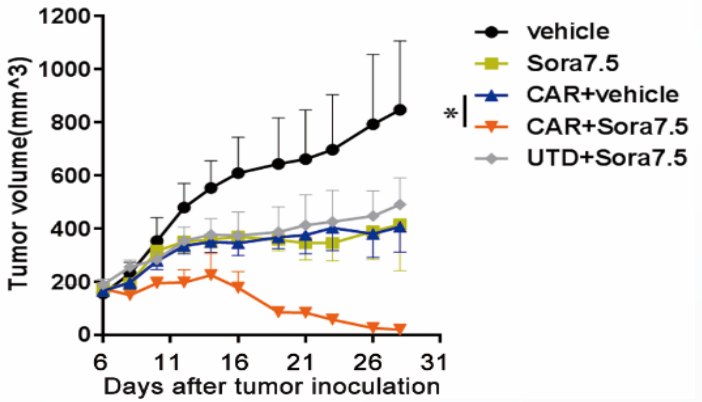
GPC3 CAR T in Combination with Sorafenib in HCC Mouse Models

Synergistic effect of CAR T cells and Tyrosine Kinase Inhibitors

- Sorafenib augmented the antitumor effects of mCAR T cells[1]
- Promoted IL-12 secretion in tumor associated macrophages (TAMs) and cancer cell apoptosis







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

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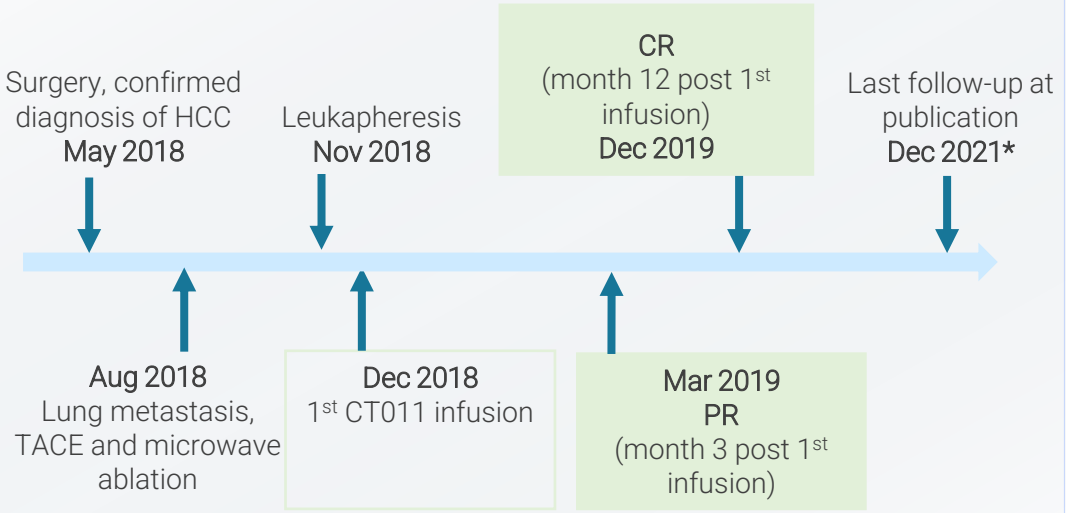
Case Report in *Frontiers in Immunology* : Complete Response and Long-term Survival (CT011 + Sorafenib for 1L HCC)

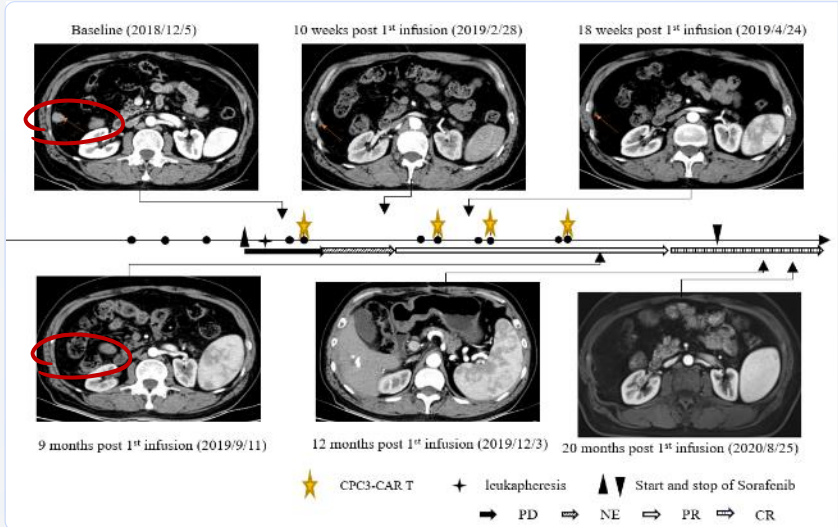
Clinical evidence supporting the curative potential of CAR T cells in early-line treatment of solid tumors[1]

NCT03302403

- A 60-year-old Asian male with HBV related HCC
- Liver recurrence and lung metastasis
- Previously treated with liver tumor resection, trans-arterial chemoembolization therapy and interventional ablation.
- GPC3 IHC test: ++ and +++ 70%

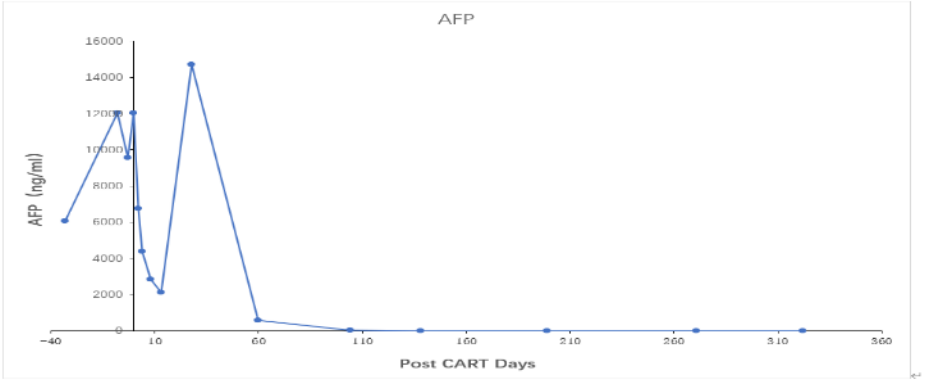


*As of Dec 2021, CR status has been over 24 months and continues



No. 3 target lesion

- ~16.76 mm at baseline
- At 9 months, this lesion completely disappeared without relapse



The AFP level declined to a normal value 3 month post 1st infusion

1. Sun, Hongwei, et al. *Frontiers in Immunology.* 13 (2022)

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Case Report in *Frontiers in Immunology* : Complete Response and Long-term Survival (CT011 + Sorafenib for 1L HCC)

The former patient is playing *Taiji* & doing exercises.

From the moment I was diagnosed with liver cancer in 2018, I received a variety of treatment methods, but none yielded the desired results. **When I got treated with CAR T-cell therapy, the situation started to change and eventually my liver cancer was cured.**

Today, I am in good health. My strength and vitality have returned to a level like before. I do regular physical activities, including walking, hiking, and swimming, a hobby of years. I even learned new swimming techniques, including freestyle, backstroke, butterfly, and diving. On average, I swim about a kilometer each day.

My quality of life is quite high, allowing me to fulfill my duties as a son to my parents too. My household has once again become a hub of energy and laughter, particularly with my two adorable granddaughters around. Filled with gratitude, I strive to give back to my family and those in need in the society.

- All the information above is subjective to the patients.
- CARsgen has obtained authorization for patients' personal information to be shared for non-promotional purposes.

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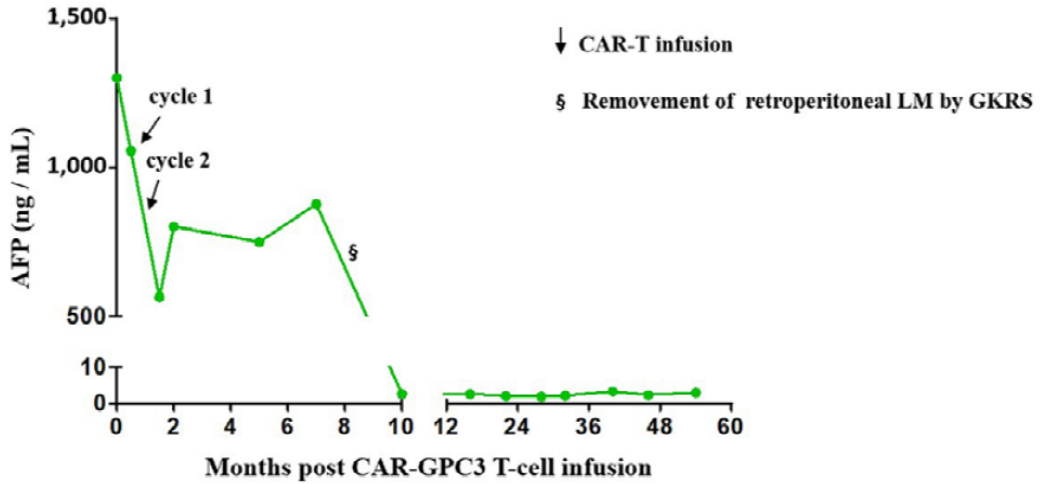
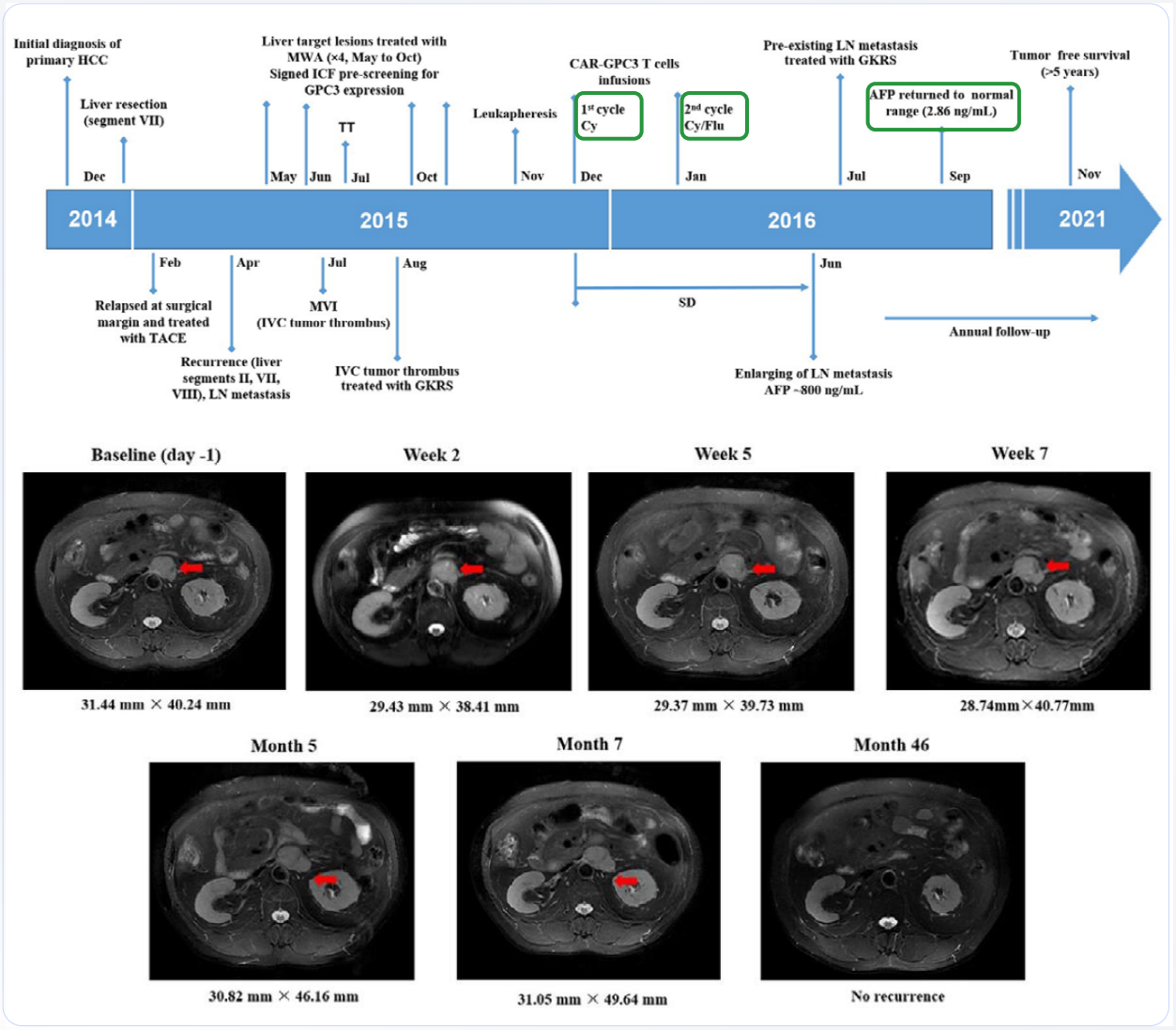
Case Report in *Cancer Communications* : Disease-free over 7 Years

NCT02395250

- A 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
- The latest follow-up date is September 4, 2023, after the publication of *Cancer Communications*





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

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Case Report in *Cancer Communications* : Disease-free over 7 Years

the former patient

I was diagnosed with liver cancer in 2014, and my condition was very poor at that time. I could not tolerate the chemotherapy very well and the cancer kept progressing despite all the therapies received. I wanted to give up but was persuaded by my family to participate in the clinical trial as the last hope. **After receiving the treatment, my condition gradually improved and got cured finally without recurrence till today.**

Not anticipating that I would survive till today, **I cherished the time and traveled to many places in China and abroad**, such as Australia, Guizhou, Yinchuan, etc. During winter, I live in Hainan in warm southern China, while during summer, I live in my hometown in cool northeastern China, just like a migrant bird.

I can participate in various activities such as fishing, playing basketball, etc. I feel that I am leading a normal life as a healthy person.

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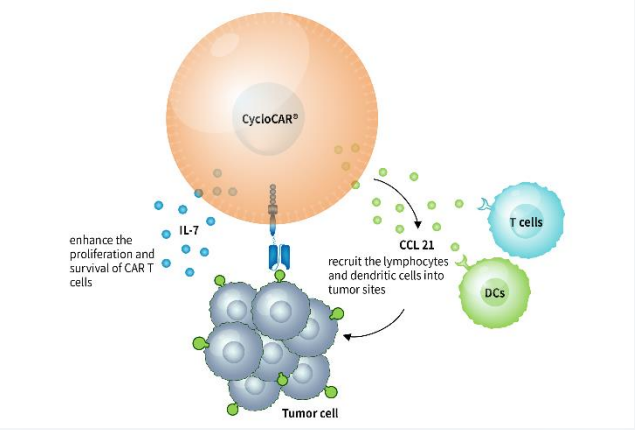
Technology Platforms

CARSGEN THERAPEUTICS

CycloCAR®: Enhanced Anti-tumor Effect and Potentially Lymphodepletion Free

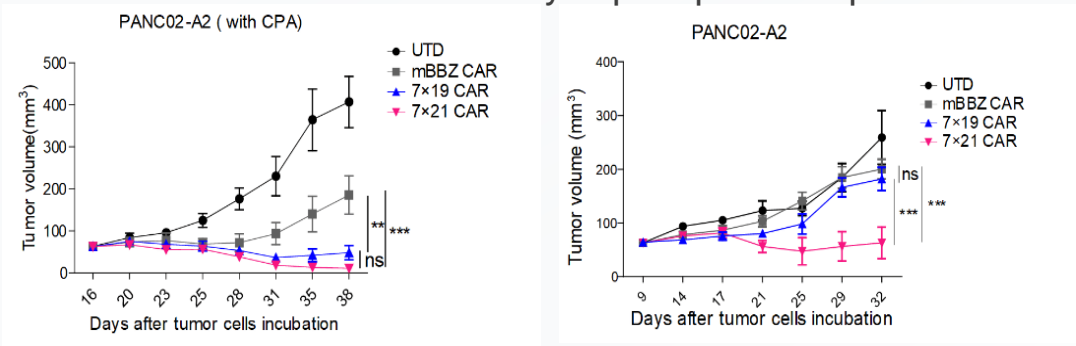
CycloCAR® (CYtokine (IL7) and Chemokine (CCL21) LOaded CAR) enables the CAR T cells to co-express IL7 and CCL21



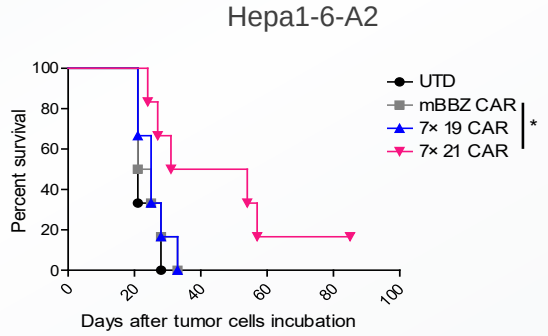
Advantages of CycloCAR® (7×21) technology:

- Increased accumulation of T cells and DC cells in tumor tissue
- Could efficiently suppress tumors with heterogeneous target expression
- Potentially lymphodepletion free

7X21 CAR T showed better antitumor activities in pancreatic cancer model with and without cyclophosphamide precondition[1]



7x21 CAR T could suppress tumor xenografts with heterogenous target expression (CLDN18.2+ and CLDN18.2- tumor cells mixed at 1:1)[1]



1. Luo H, et. al. *Clinical Cancer Research.* 2020 Oct 15;26(20):5494-5505

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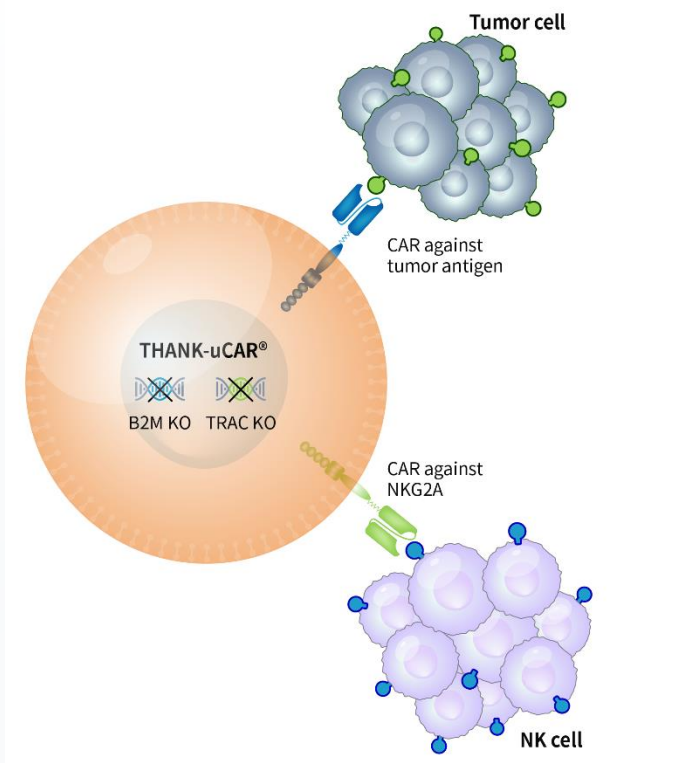
THANK-uCAR®: Market-Differentiating uCAR T Platform to Address Immune Evasion

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



Allogeneic universal CAR (uCAR) T cells must evade rejection by the host immune system, or HvGR

- 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

HvGR: host versus graft reaction
GvHD: graft versus host disease

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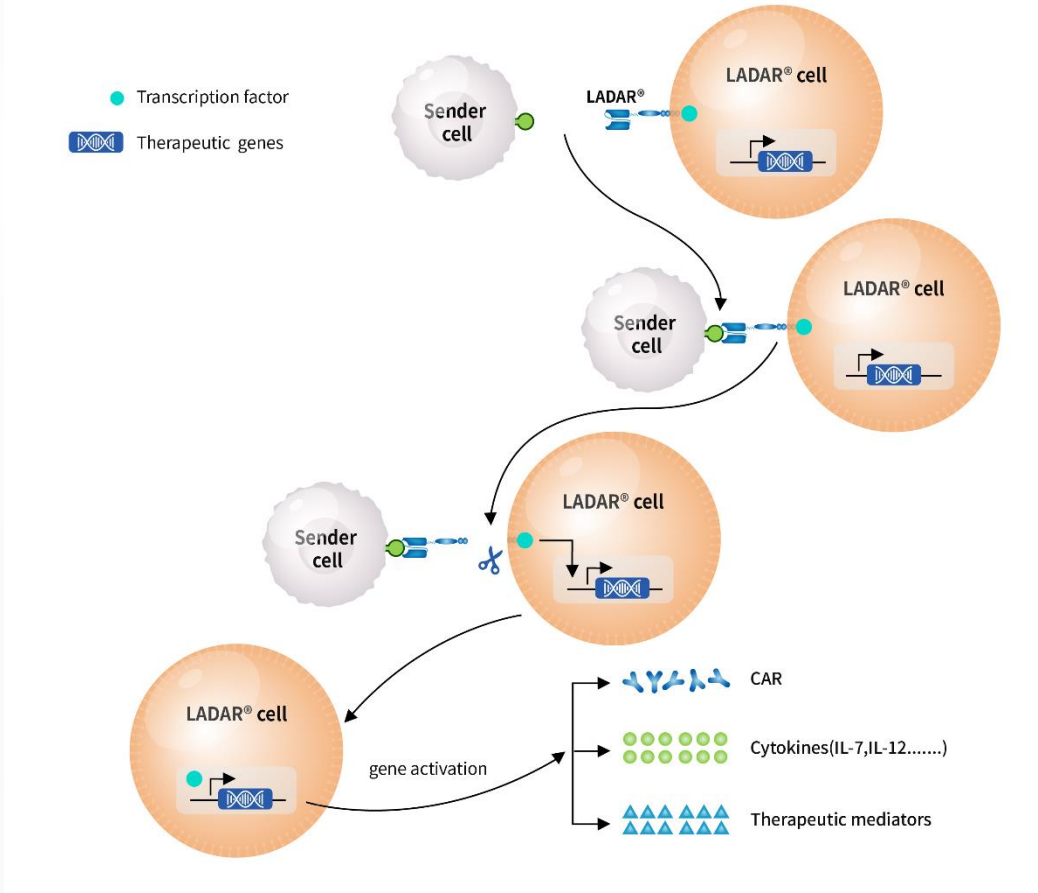
LADAR®: A Powerful Technology for Precise Targeting



LADAR®: Local Action Driven by Artificial Receptor

LADAR® is an artificial receptor that only induces the therapeutic protein expression in the presence of the LADAR ligand, leading to local antitumor activity, thereby:

- Significantly reducing the risk of side effects, such as on-target off-tumor toxicities
- Potentially making more targets available for cell therapies

Advantages over SynNotch[1,2]:

- LADAR® is smaller than SynNotch (sparing additional room for >200 amino acids)
- Significantly higher sensitivity to low-level sender antigen expression

1. Morsut L, et. al. *Cell.* 2016 Feb 11;164(4):780-91
2. Roybal KT, et. al. *Cell.* 2016 Oct 6;167(2):419-432

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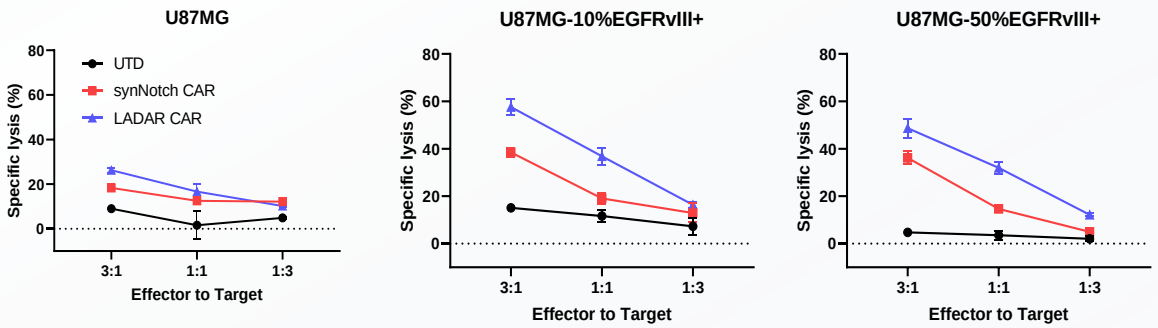
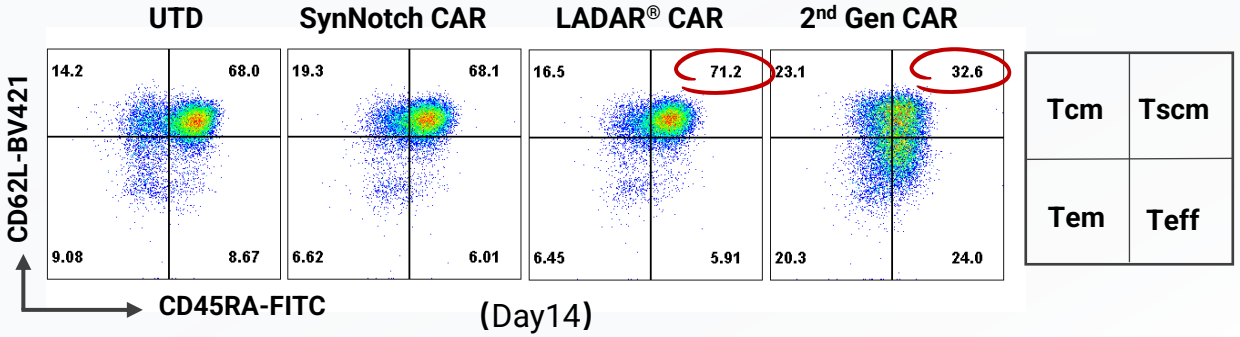
LADAR®: A Powerful Technology to Address On-target Off-tumor Toxicity, or Systemic Toxicity of Therapeutic Proteins

Stronger cytotoxicity than SynNotch



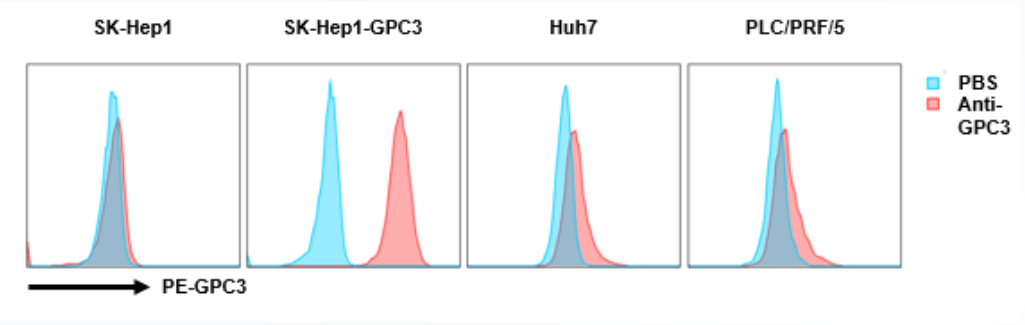
High fraction of LADAR® T cells remain as stem memory T cells

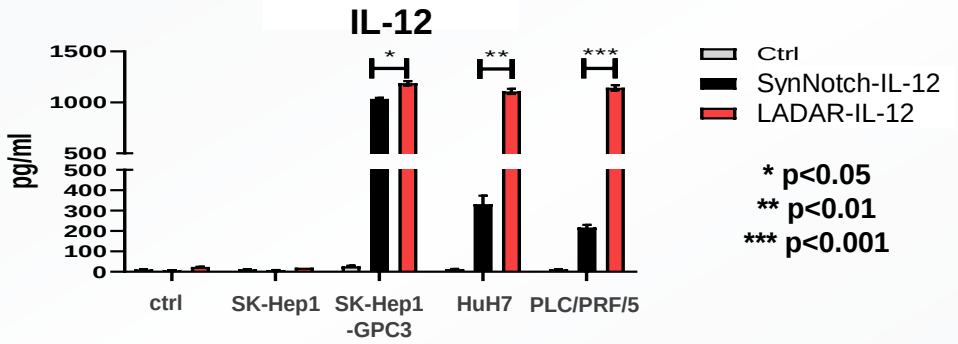


(Day14)

α-EGFRvIII LADAR-α-IL13Rα2 CAR

Higher sensitivity to low level of antigen





LADAR® T cells induced IL-12 expression 4-6–fold the level produced by SynNotch T cells in the presence of low-level GPC3 expression

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External Partnerships

Commercialization Collaboration

- Partner 华东医药股份有限公司 HUADONG MEDICINE CO.,LTD. (SZ: 000963)
- Product Zevor-cel (BCMA CAR T)
- Territory Mainland China
- Rights Exclusive commercialization
- Upfront payment RMB200 million
- Regulatory and commercial milestone payments up to RMB1,025 million
- CARsgen will continue to be responsible for the development, regulatory approval, and manufacturing of CT053 in mainland China.

Co-development

- Partner moderna (NASDAQ: MRNA)
- Product CT041 (Claudin18.2 CAR T)
- Preclinical studies and a phase I clinical trial to evaluate CT041 in combination with Moderna's Claudin18.2 mRNA cancer vaccine.

License Agreement

- Licensee inno.N (KOSDAQ: 195940)
- Products
  CT032 (CD19 CAR T)
  CT053 (BCMA CAR T)
- Territory the Republic of Korea
- Milestone payments USD50 million
- Royalties up to double digit percentage on net sales

Continue to establish additional external partnerships with leading research institutes and pharmaceutical companies on technology and product licenses

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Making Cancer Curable

CARSGEN
THERAPEUTICS