



# Gracell Biotechnologies

Pioneering the Next Generation  
of CAR-T Cell Therapies

**Corporate Presentation | AUGUST 2021**

GRCL (NASDAQ) | [gracellbio.com](http://gracellbio.com)

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# Gracell At A Glance

We are a global clinical-stage biopharmaceutical company dedicated to discovering and developing breakthrough cell therapies to address major industry challenges and fulfill unmet medical needs in the treatment of cancer. We aim to disrupt conventional approaches to CAR-T cell therapies with our proprietary technology platforms—FastTCAR and TruUCAR.

## Key Financial Highlights

Cash & short term investments	\$318 M (as of 6/30/21)
ADS Outstanding (as converted*)	~67.3 M (as of 6/30/21)
Net proceeds from IPO	\$220 M

## Key Company Highlights

Nasdaq	GRCL
History	Founded In 2017
Headquarter	China
Operations	China and US

\* Each of our ADS represents five ordinary shares. In addition to the issued and outstanding ordinary shares, as of June 30, 2021, 11,707,435 options were granted and 10,946,710 options were outstanding, and 303,030 restricted share units ("RSUs") were granted under our employee stock option plan.



# Proprietary Technology Platforms and Enhancements



Technology platforms  
to improve treatment  
outcomes & overcome  
industry commercial  
bottlenecks

Proprietary  
technology toolkit to  
enhance platforms

## ***asT CAR***

### **Autologous CAR-T Platform**

- Next-day manufacturing
- Younger T-cells with enhanced fitness
- Fully-closed manufacturing capabilities

## ***TruUCAR***

### **Allogeneic CAR-T Platform**

- Off-the-shelf availability
- Novel design to eliminate HvG without need of extra immunosuppressive therapeutics

## ***Dual CAR***

- Deep expertise in protein chemistry
- True dual-antigen targeting
- Leverage a second CAR to reduce rejection

## ***Enhanced CAR***

- To overcome immunosuppressive tumor microenvironment
- To regulate cytokine signaling

# Global Clinical Development Pipeline



	Program	Indication	Phase of Development				Milestones / Anticipated Milestones
			Preclinical	Phase 1	Phase 2	Phase 3	
FasTCAR	GC012F BCMA/CD19	RR MM	<div>China IIT Ongoing*</div>				U.S. IND filing: 1H 2022** China IND filing: 1H 2022
	GC019F CD19	Adult B-ALL	<div>China IIT Completed*</div>				China IND approved
			<div>China IND Approved</div>				
	Dual-target Product Candidates	B-NHL	<div></div>				
TruUCAR	GC027 CD7	Adult T-ALL Other	<div>China IIT* Ongoing</div>				U.S. IND filing: 2022** China IND filing: 2022
Donor-derived CAR	GC007g CD19	B-ALL	<div>China IIT * Completed</div>				China IND approved - seamless Phase 1/2 registrational study
			<div>China IND Phase 1/2 Study Ongoing</div>				

\* IIT (investigator-initiated trial) is optional not mandatory, and it serves as early evidence for safety and potentially efficacy for the individual programs. IND studies will build on IIT results.

\*\* We intend to use the clinical data generated from China IITs in our IND filings to the FDA and the NMPA; however, we make no guarantee that such data will be accepted by the FDA and/or the NMPA.

RR MM, relapsed or refractory multiple myeloma; B-ALL, B cell acute lymphoblastic leukemia; B-NHL, B cell non-Hodgkin's lymphoma; T-ALL, T cell acute lymphoblastic leukemia

# GC007g for B-ALL: Pivotal Phase 1/2 Study Approved by NMPA



## IND registrational study is open in China

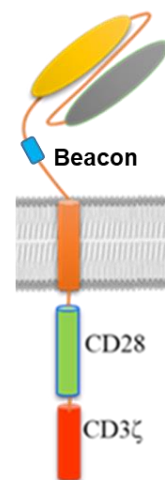
### NMPA approved in December 2020

- Seamless Phase 1b/2 registrational study
- Several site initiation visits completed – study accruing patients
- First dosing cohort completed

## Clinical IIT Update as of June 2019 (n = 13)

Efficacy	DL1 (n=3)	DL2 (n=9)	DL3 (n=1)	Overall (n=13)
ORR (D28)	3 (100%)	7 (77.8%)	1 (100%)	11 (84.6%)
MRD- (D28)	3 (100%)	6 (66.7%)	1 (100%)	10 (76.9%)

- T cells from HLA-matched healthy donor
- Indication: R/R B-ALL patients who progress or failed transplant
  - Healthy donor derived T-Cells
  - GC007g as allogeneic therapy is readily available for treatment
    - No need for leukapheresis
- Alternative for patients ineligible for other treatment options

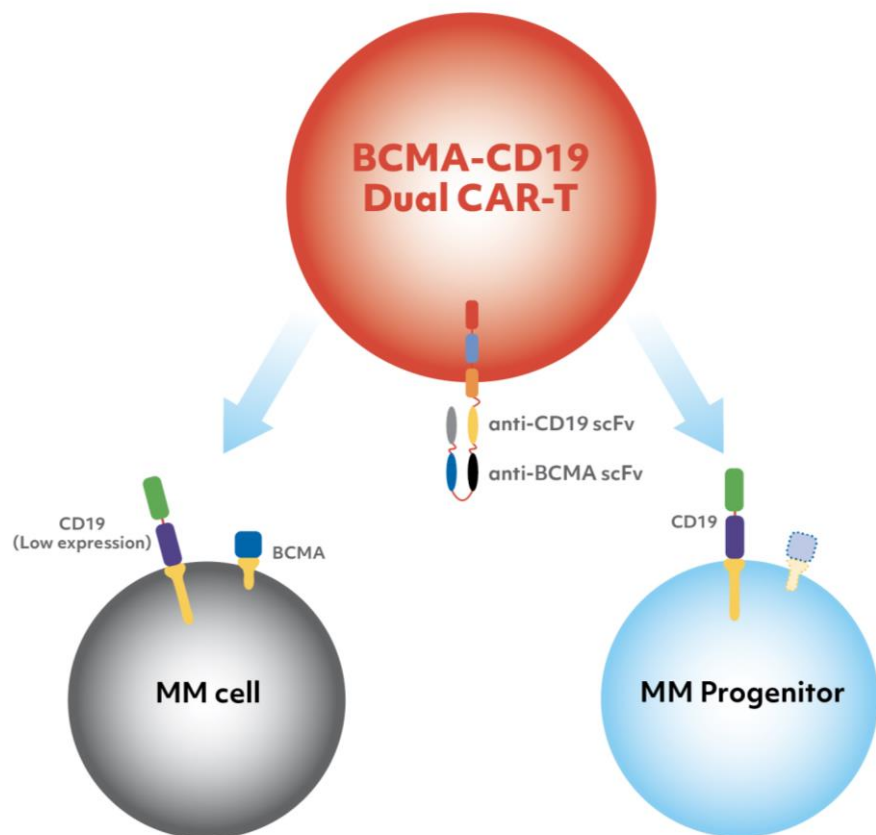


Safety	DL1 (n=3)	DL2 (n=9)	DL3 (n=2)	Overall (n=14)
CRS	1 (33.3%)	9 (100%)	2 (100%)	12 (85.7%)
≥ 3 CRS	0	1 (11.1%)	0	1 (7.1%)
NT	0	0	0	0
≥ 3 NT	0	0	0	0
aGvHD	0	2 (22.2%)	0	2 (14.3%)

\* NMPA, National Medical Products Administration

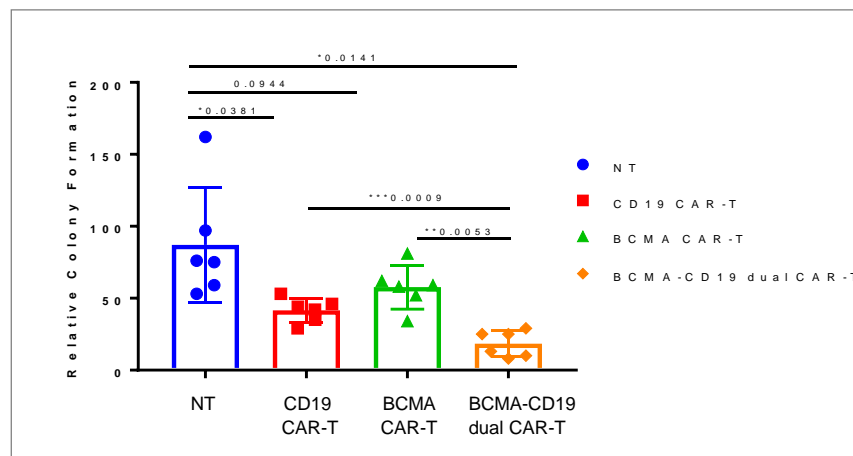
# GC012F: Rationale for Dual-Targeting for Multiple Myeloma

## DUAL targeting BCMA/CD19 for MM



## Targeting Both Antigens in MM is Designed to Drive Fast, Deep and Durable Responses in MM Patients

- BCMA is universally expressed on malignant plasma cells<sup>1</sup>
- CD19 is expressed on both multiple myeloma (MM) cells and their progenitors<sup>2</sup>
- Targeting CD19 can trigger elimination of malignant cells by CAR-T<sup>3</sup>



Our preclinical work demonstrated more effective elimination of MM clone-forming cells by BCMA/CD19 Dual CAR-T<sup>4</sup>

1. Tai YT, Anderson KC. Immunotherapy. 2015;7(11):1187-1199.
2. Boucher K, Parquet N, Widen R, et al. Clin Cancer Res. 2012;18(22):6155-6168.
3. Nerretter T, Letschert S, Götz R, et al. Nat Commun. 2019;10(1):3137.
4. Hua Jiang, et al. ASH Annual Meeting 2020, 178



# GC012F: Dual BCMA-CD19 CAR-T for Multiple Myeloma



Ongoing Phase 1 multicenter IIT study in China

Interim data presented ASH 2020 / ASCO 2021 / EHA 2021

n = 19 patients

CAR-T cells were administered in a single infusion at 3 dose levels  $1 \times 10^5/\text{Kg}$  (DL1) (1 patient),  $2 \times 10^5/\text{Kg}$  (DL2) (9 patients) and  $3 \times 10^5/\text{Kg}$  (DL3) (9 patients).

## High Risk\* Multiple Myeloma

- **94.7% (n=18) of the IIT population were patients with high-risk features**
- High risk patients comprise 20-30% of the overall MM population across all lines of therapy
- Subset of patients that are extremely difficult to treat

\* Defined by mSMART 3 criteria



# GC012F DUAL CAR-T for MM: Study Design



## Multicenter, open-label, single-arm IIT<sup>1</sup> study

### ➤ Key Eligibility Criteria

- Relapsed/Refractory Multiple Myeloma (IMWG criteria 2016)
- Expected survival  $\geq 3$  months
- Adequate organ function

### ➤ Primary endpoint:

- Adverse Events

### ➤ Secondary endpoints:

- MRD at pre-specified timepoints post CAR-T infusion
- ORR
- PFS, OS and DOR at 3 months and 6 months after CAR-T infusion
- PK of CAR-T cells

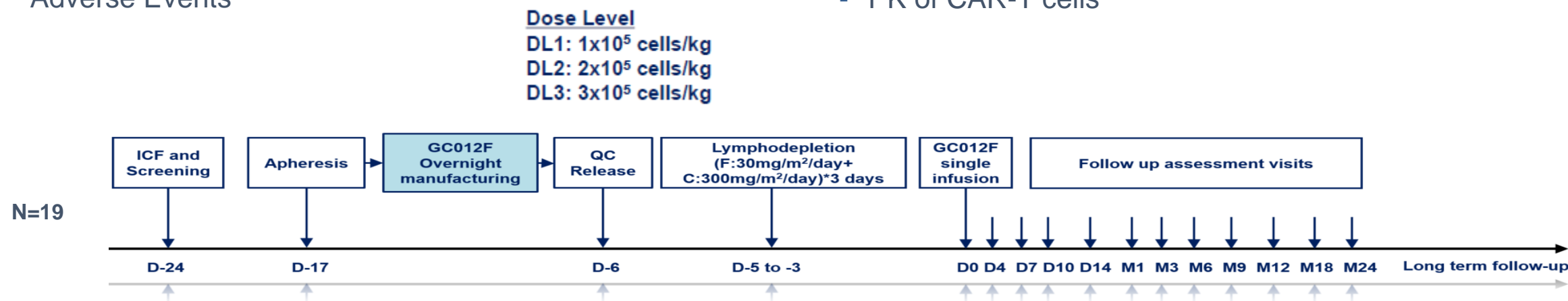


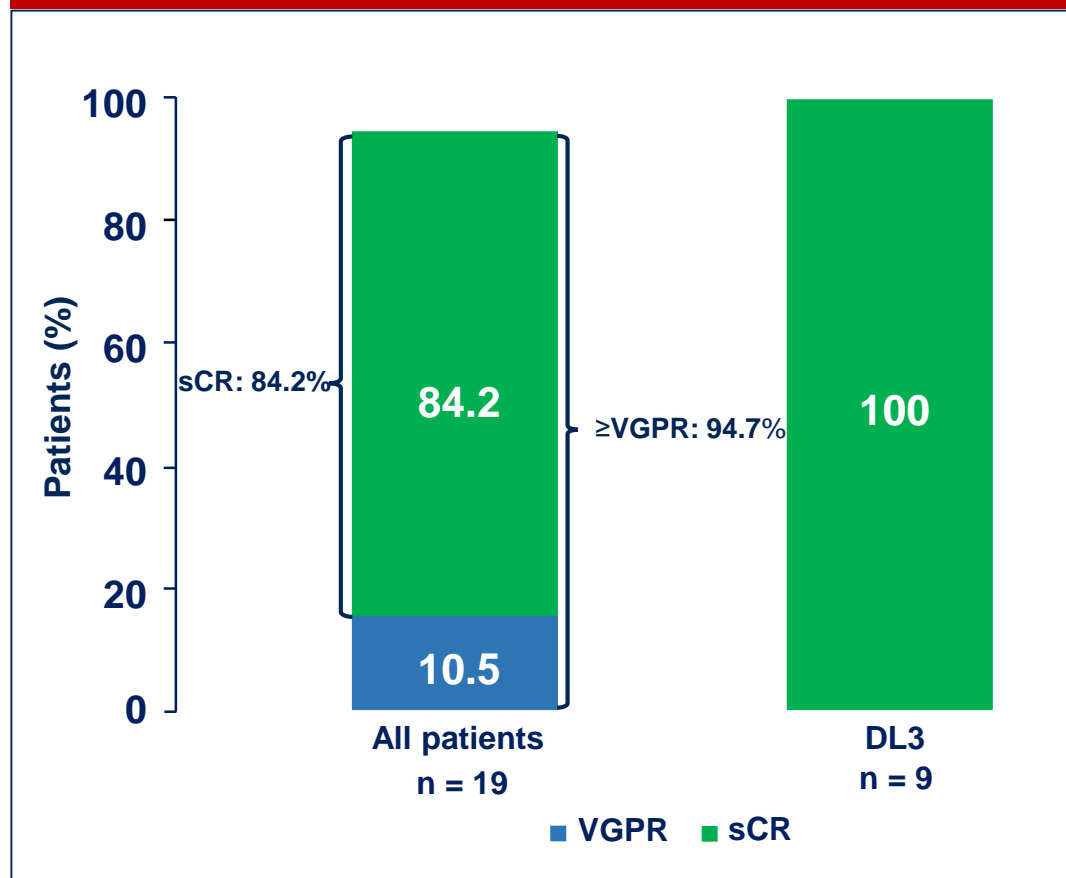
Fig 1. Study schema

<sup>1</sup>IIT – investigator initiated trial

MRD, minimal residual disease; ORR, overall response rate; PFS, progression-free survival; OS, overall survival; DOR, duration of response; PK, pharmacokinetics

# GC012F DUAL CAR-T for MM: Response Assessment

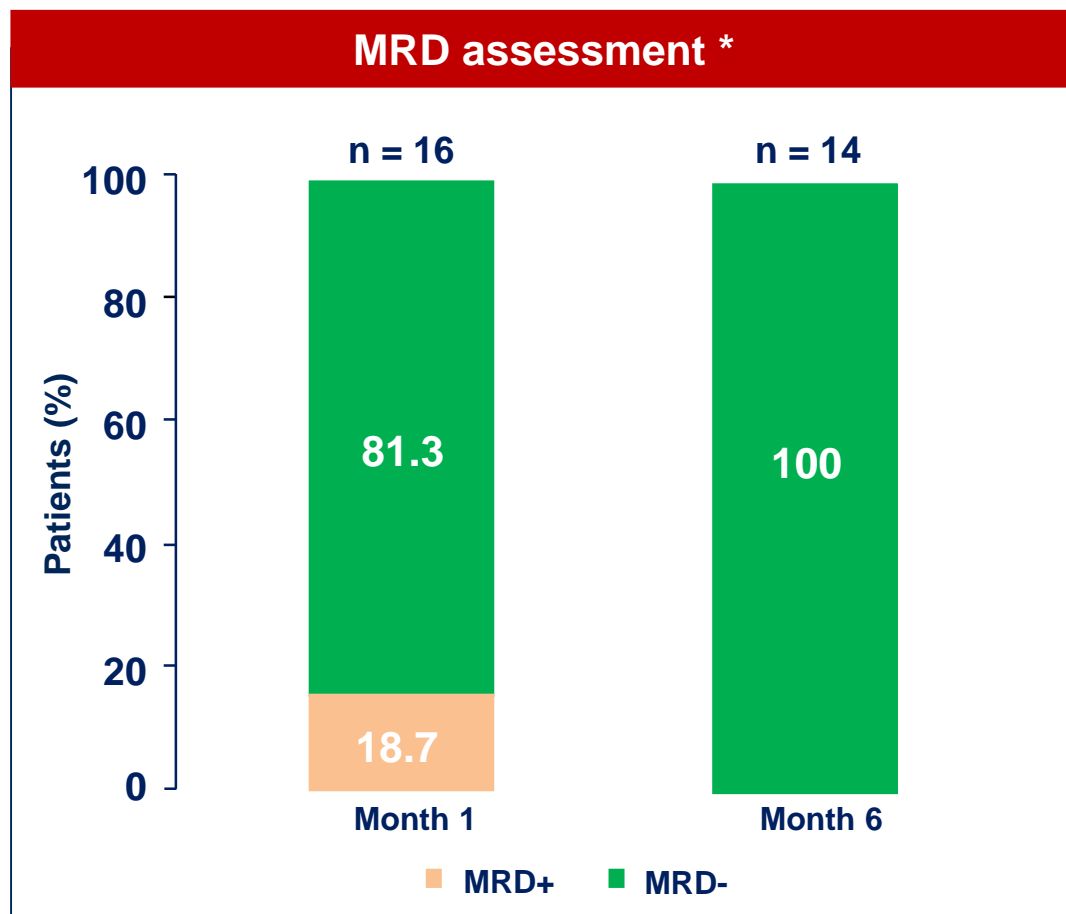
ORR = at time of data cut-off January 12, 2021



- Time to earliest response: 28 days
- ORR = 94.7% (18/19) patients
- Best response achieved to date
  - ✓ CR/sCR – 84.2% (16/19)
  - ✓ VGPR or better – 94.7% (18/19)
  - ✓ **9 out of 9 (100%) achieved sCR in DL3**
- Median duration of response (DOR) not yet reached

sCR, stringent complete response; CR, complete response, VGPR, very good partial response

# GC012F DUAL CAR-T for MM: Minimal Residual Disease

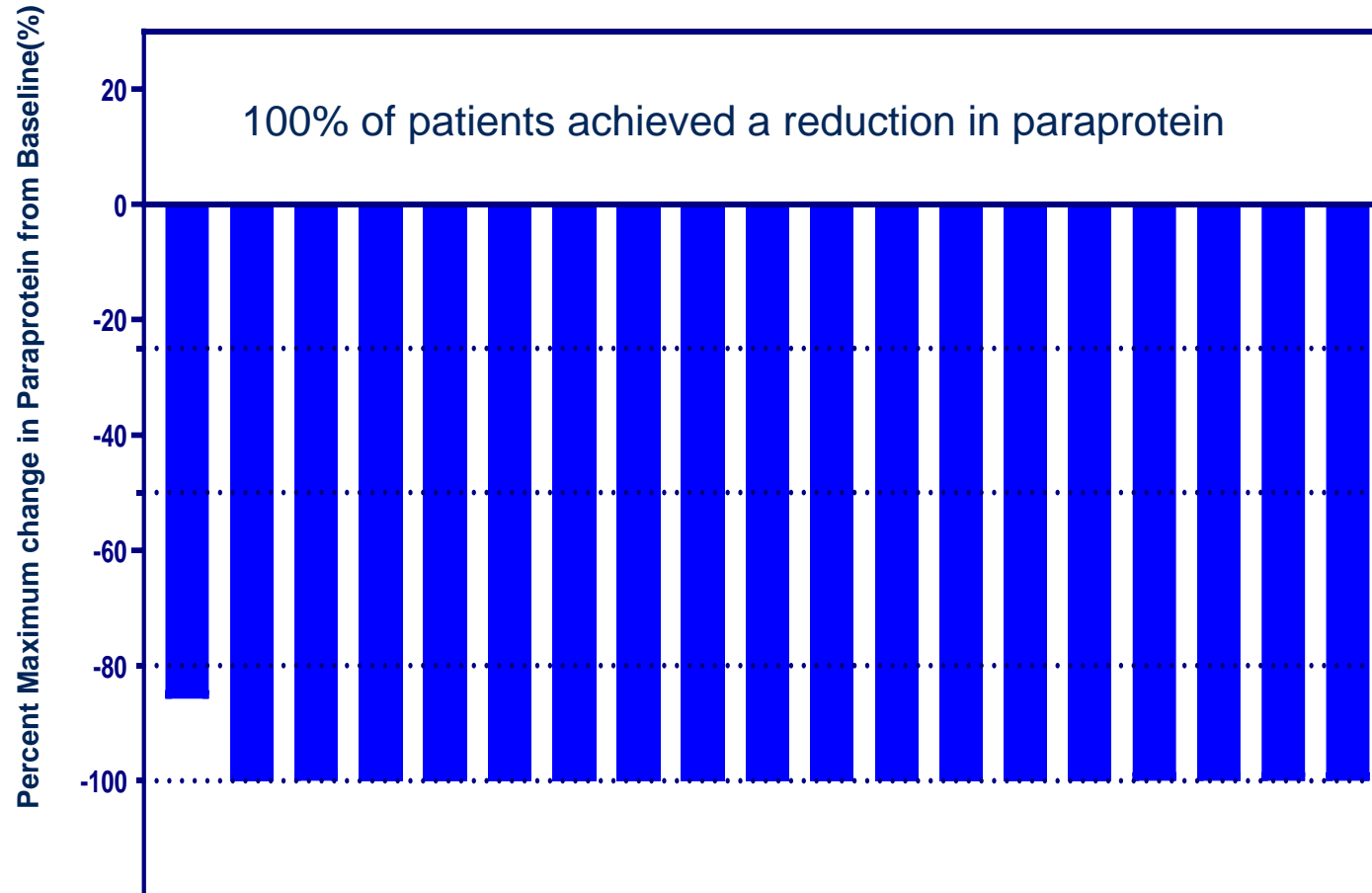


- All patients had at least one post-baseline bone marrow sample available for MRD assessment by NGF (Next Generation Flow)
- 100% of evaluable patients were MRD negative at Month 6 (n=14)

\*Sensitivity of MRD- :

- At  $10^{-4}$  in 7 patients tested by Flow cytometry
- At  $10^{-6}$  in 12 patients tested by EuroFlow

# GC012F DUAL CAR-T for MM: Paraprotein and Tumor Burden Reduction



- Maximum Reduction in Tumor Burden from Baseline in Response-Evaluable Patients (n=19)
- All patients achieved a reduction in paraprotein (n=19)

Paraprotein: serum M-protein, urine M-protein, or difference between involved and involved free light chain (dFLC) for patients with light chain only measurable

## GC012F showed very promising activity in R/R MM patients

- High Risk patients (18/19, 94.7%) as defined by mSMART3.0
- Patients heavily pretreated including anti-CD38 mAb, PI, and IMiD
  - Median of 5 prior lines of therapy

### GC012F showed

- ✓ **94.7% ORR VGPR or better (sCR)**
- ✓ 100% patients achieving sCR or VGPR as best response were evaluated to be MRD negative
- ✓ 100% MRD negative sCR rate in DL3 (n=9)

### Favorable Safety Profile

- ✓ CRS Grade 0 1/19 (5.26%), CRS Grade 1/2 16/19 (84.2%), Grade 3 in 2/19 (10.5%) patients
- ✓ No CRS Grade 4/5 observed
- ✓ **No ICANS observed**

# TruUCAR: Unique Design to Prevent HvG

TruUCAR is a proprietary technology platform for generating high-quality allogeneic CAR-T therapies that use T cells from non-HLA matched healthy donors, and can be made in large quantities as “off-the-shelf” and “ready-to-use” products at lower cost

## Challenge With Conventional Allogeneic Car-T

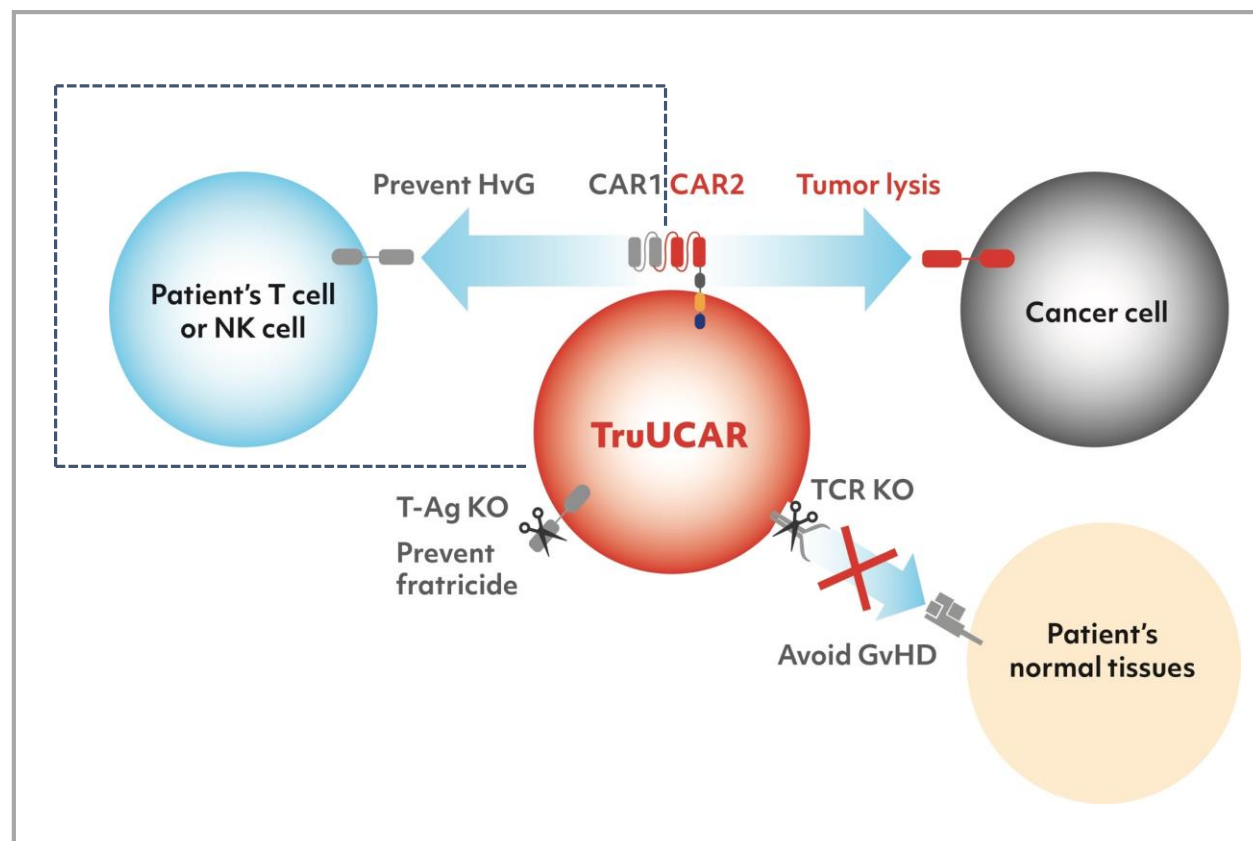
Major challenge in developing a safe and effective UCAR-T is the host vs graft rejection (HvG)

## Novel Design To Reduce Risk Of Patient Rejection

TruUCAR-enabled CAR-T therapy prevents HvG through novel design of a dual-function CAR or a second CAR targeting patient's T and NK cells

## Stand-alone Therapy

Eliminating need of combination therapy with additional potent immunosuppressant to induce deeper immune suppression, TruUCAR-enabled CAR-T therapies can be administered as a stand-alone therapy and provide potential benefits in cost-savings and safety



# GC027: Clinical Data in T-cell Acute Lymphoblastic Leukemia (T-ALL)



## R/R T-ALL- A High Unmet Medical Need

- ~64,000 patients diagnosed with ALL annually
  - ~6,000 T-ALL expected to be diagnosed in U.S. in 2020
- T-ALL accounts for approx. 25% of ALL in adults <sup>1</sup>
- High unmet medical need
  - Standard chemotherapy regimens only result in 30% - 40% response rate with 6 months median Overall Survival among responders
- Highly aggressive, most patients relapse within 2 years
- Relapsed patients have dismal prognosis with very limited treatment options and <10% of patients surviving beyond 5 years <sup>1</sup>

## TruUCAR GC027

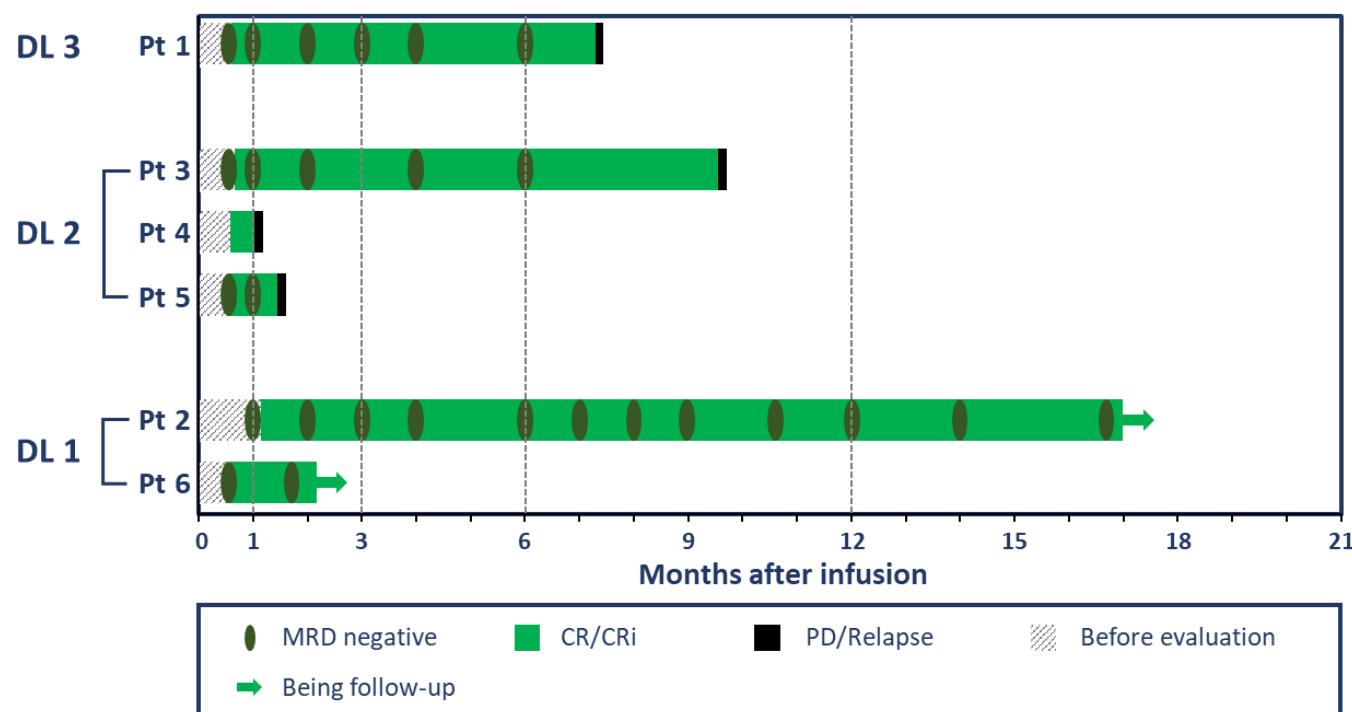
- **Preclinical comparison to conventional UCAR-T**
  - Comparable in vitro cancer cell killing
  - Superior Fold Expansion after Antigen Stimulation
  - Superiority in in vivo engraftment and anti-Leukemia effects (murine Xenograft model)
- **Phase 1 single arm open label multi-center IIT study in China**
  - Primary endpoint safety
  - Secondary endpoint efficacy
- Data cut off Feb. 2021, 6 adult r/r T-ALL pts enrolled and treated
- AACR 2020 / EHA 2020 / AACR 2021

1. D.I. Marks, C. Rowntree, Management of adults with T-cell lymphoblastic leukemia, Blood 2017



# GC027 for T-ALL: Fast and Deep Responses

Response, Duration of Remission and Adverse Events, as of February 2021 (n=6)



## Efficacy

- 100% CR/CRi (6/6)
- 83% MRD-CR/CRi (5/6)
- Median PFS: 7.75 months
- The longest DOR (MRD-CR): 16.8 months

## Safety

- All 6 patients tolerated infusion of GC027
- No ICANs observed (Immune effector cell-associated neurotoxicity)
- No evidence of GvHD
- 6/6 patients experienced CRS, no Grade 5 CRS
- AEs were reversible

Lei Gao , et al. AACR Annual Meeting 2021, LB147

MRD, minimal residual disease, CR complete response, CRi, complete response with incomplete hematologic recovery, PD, progressive disease

	PROGRAM	INDICATION
FasTCAR	Dual-target Product Candidates	B-NHL
	GC008E	Solid tumors (ovarian cancer or breast cancer)
TruUCAR	GC502	B cell malignancies
	GC202	PTCL
	GC207	T-ALL,T-LBL
	GC212	MM

# State-of-the-art R&D and GMP Facilities



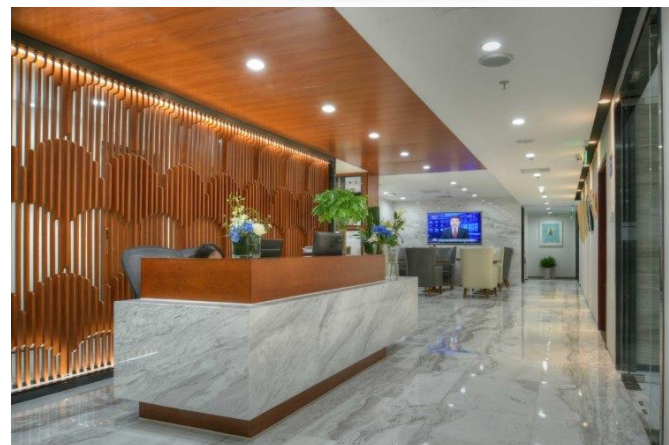
Shanghai R&D 14,900 SQF



Suzhou GMP 66,000 SQF



Shanghai R&D 45,500 SQF



Beijing Office

- GMP manufacturing facility in Suzhou, China
  - Plasmid, vectors and cell production
  - Vein-to-vein fully-closed manufacturing capability
  - Global compliance of cell and gene therapy product development and manufacturing
  - Received *Medical Products Manufacturing Certificate* in 2021
  - Reserved commercial blueprint
- R&D centers in Shanghai, China
- Commenced operations in the U.S.

# Financial Highlights

Strong financial position to support R&D and corporate strategies



## CASH

Cash & short term  
investments of \$318 M  
on June 30<sup>th</sup>, 2021



## R&D and Corporate Strategies

Well-financed to fund:

- Clinical development to advance key programs including GC012F for MM and GC027 for T-ALL
- Expansion of GMP manufacturing facilities in Suzhou
- Launch of US R&D center

# 2021-2022 Targets

Jan 2021	✓ GC019F for r/r B-ALL IND Approval in China
Mar 2021	✓ Selection of Lonza as the US CDMO to support US IND filing
Mar 2021	✓ Enrollment of first patient in GC007g for B-ALL Ph1/2 registrational study in China
Apr 2021	✓ GC027 for T-ALL clinical data update at AACR 2021 Annual Meeting
Jun 2021	✓ GC012F for multiple myeloma clinical data update at ASCO and EHA 2021 Annual Meetings
2H 2021	Tech transfer to Lonza to support GC012F US IND filing
	Progress of early pipeline into clinical studies
	Expansion of state-of-the-art Suzhou GMP facilities with fully-closed production capabilities
	Establishing R&D facilities in the U.S.
1H 2022	GC012F IND filing in both U.S. and China
2022	GC027 IND filing in both U.S. and China

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