Legend Biotech

2022 R&D Day

October 3, 2022

Forward-looking Statements

Statements in this report about future expectations, plans and prospects, as well as any other statements regarding matters that are not historical facts, constitute "forward-looking statements" within the meaning of The Private Securities Litigation Reform Act of 1995. These statements include, but are not limited to, statements relating to Legend Biotech's overall strategies and objectives; Legend Biotech's ability to achieve milestones under its collaboration with Janssen Biotech; Legend Biotech's strategy and plans for the development, manufacturing and commercialization of ciltacabtagene autoleucel (cilta-cel), including anticipated regulatory milestones; the preclinical and clinical development strategy for product candidates and the anticipated timing of key regulatory and clinical milestones for such product candidates; the potential benefits afforded by investigational candidates; and the opportunities represented by preclinical data. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "will," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors. Legend Biotech's expectations could be affected by, among other things, uncertainties involved in the development, manufacturing and commercialization of new pharmaceutical products; unexpected or inconsistent preclinical data; unexpected clinical trial results, including as a result of additional analysis of existing clinical data or unexpected new clinical data; unexpected regulatory actions or delays, including requests for additional safety and/or efficacy data or analysis of data, or government regulation generally; unexpected delays as a result of actions undertaken, or failures to act, by our third party partners; uncertainties arising from challenges to Legend Biotech's patent or other proprietary intellectual property protection, including the uncertainties involved in the US litigation process; competition in general; government, industry, and general public pricing and other political pressures; the duration and severity of the COVID-19 pandemic and governmental and regulatory measures implemented in response to the evolving situation; as well as the other factors discussed in the "Risk Factors" section of the Company's Annual Report on Form 20-F filed with the Securities and Exchange Commission on March 31, 2022. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those described in this report as anticipated, believed, estimated or expected. Legend Biotech specifically disclaims any obligation to update any forward-looking statement, whether as a result of new information, future events or otherwise. In addition, caution should be exercised when interpreting results from separate trials involving separate product candidates. There are differences in the clinical trial design, patient populations, and the product candidates themselves, and the results from the clinical trials of distinct product candidates may have no interpretative value with respect to our existing or future results. Similarly, caution should be exercised when interpreting results relating to a small number of patients or individually presented case studies.

Forward-looking Statements

The safety and efficacy of the agents and/or uses under investigation that will be discussed today have not been established. There is no guarantee that the agents will receive health authority approval or become commercially available in any country for the uses being investigated.

Agenda

Welcome	**Joanne Choi, Investor Relations**	**10:00 a.m. – 10:05 a.m.**
Introduction	Dr. Ying Huang, CEO	10:05 a.m. – 10:15 a.m.
Global BCMA Program	Dr. Lida Pacaud, VP, Clinical Development Steve Gavel, VP, Commercial Development, US & Europe	10:15 a.m. – 11:00 a.m.
Coffee Break		**11:00 a.m. – 11:15 a.m.**
Research & Development • Strategy • Solid Tumors • Allogeneic Programs	Dr. Guowei Fan, Global Head of Research and Early Development	11:15 a.m. – 12:15 p.m.
Q&A		**12:15 p.m. – 1:00 p.m.**
Conclusion		**1:00 p.m. – 1:05 p.m.**

Introduction

Ying Huang, Ph.D.
Chief Executive Officer

Our Presenters

Lida Pacaud, M.D.

Vice-President, Clinical Development

A trained physician, Dr. Lida Pacaud formerly led the CART Global Clinical Program at Novartis and served as the Executive Medical Director of its Cell & Gene Unit.

Steve Gavel

Vice-President, Commercial Development

Steve Gavel has spent 20 years conducting commercial and marketing in the biotechnology industry. At Celgene, Steve headed commercial development activities for the bb2121 program.

Guowei Fang, Ph.D.

Senior Vice President, Research & Early Development

Dr. Guowei Fang is an accomplished scientist and pharmaceutical leader in research and development. Dr. Fang recently joined Legend from Zymeworks and Pharmacyclics.

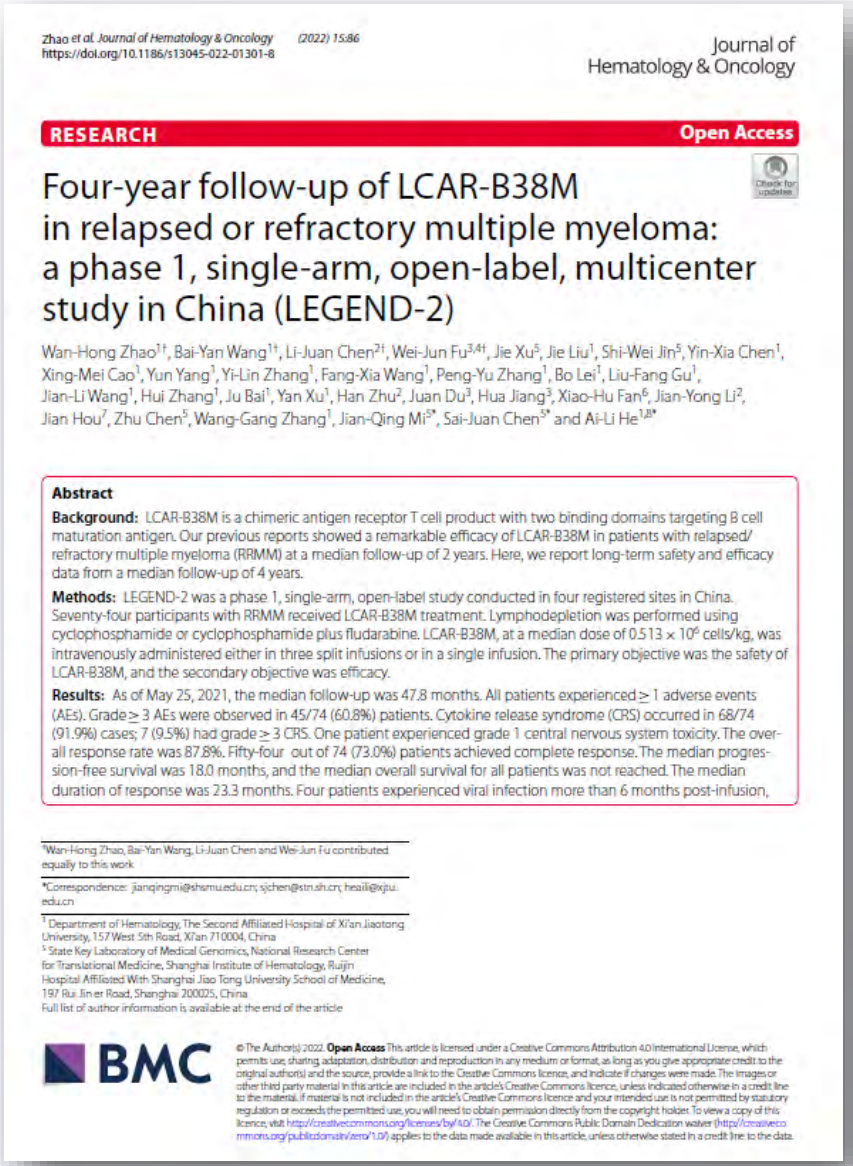
LEGEND BIOTECH

Advancing Treatment Options for Multiple Myeloma

Lida Pacaud, M.D.
Vice President of Clinical Development

Steve Gavel
Vice President of Commercial Development, US and Europe

LEGEND-2: 4-year follow-up publication



Zhao et al. Journal of Hematology & Oncology (2022) 15:86
https://doi.org/10.1186/s13045-022-01301-8

Journal of Hematology & Oncology

RESEARCH Open Access

Four-year follow-up of LCAR-B38M in relapsed or refractory multiple myeloma: a phase 1, single-arm, open-label, multicenter study in China (LEGEND-2)

Wan-Hong Zhao[1†], Bai-Yan Wang[1†], Li-Juan Chen[2†], Wei-Jun Fu[3,4†], Jie Xu[5], Jie Liu[1], Shi-Wei Jin[5], Yin-Xia Chen[1], Xing-Mei Cao[1], Yun Yang[1], Yi-Lin Zhang[1], Fang-Xia Wang[1], Peng-Yu Zhang[1], Bo Lei[1], Liu-Fang Gu[1], Jian-Li Wang[1], Hui Zhang[1], Ju Bai[1], Yan Xu[1], Han Zhu[2], Juan Du[3], Hua Jiang[3], Xiao-Hu Fan[6], Jian-Yong Li[2], Jian Hou[7], Zhu Chen[5], Wang-Gang Zhang[1], Jian-Qing Mi[5*], Sai-Juan Chen[5*] and Ai-Li He[1,8*]

Abstract

Background: LCAR-B38M is a chimeric antigen receptor T cell product with two binding domains targeting B cell maturation antigen. Our previous reports showed a remarkable efficacy of LCAR-B38M in patients with relapsed/refractory multiple myeloma (RRMM) at a median follow-up of 2 years. Here, we report long-term safety and efficacy data from a median follow-up of 4 years.

Methods: LEGEND-2 was a phase 1, single-arm, open-label study conducted in four registered sites in China. Seventy-four participants with RRMM received LCAR-B38M treatment. Lymphodepletion was performed using cyclophosphamide or cyclophosphamide plus fludarabine. LCAR-B38M, at a median dose of 0.513×10^6 cells/kg, was intravenously administered either in three split infusions or in a single infusion. The primary objective was the safety of LCAR-B38M, and the secondary objective was efficacy.

Results: As of May 25, 2021, the median follow-up was 47.8 months. All patients experienced ≥ 1 adverse events (AEs). Grade ≥ 3 AEs were observed in 45/74 (60.8%) patients. Cytokine release syndrome (CRS) occurred in 68/74 (91.9%) cases; 7 (9.5%) had grade ≥ 3 CRS. One patient experienced grade 1 central nervous system toxicity. The overall response rate was 87.8%. Fifty-four out of 74 (73.0%) patients achieved complete response. The median progression-free survival was 18.0 months, and the median overall survival for all patients was not reached. The median duration of response was 23.3 months. Four patients experienced viral infection more than 6 months post-infusion,

†Wan-Hong Zhao, Bai-Yan Wang, Li-Juan Chen and Wei-Jun Fu contributed equally to this work

*Correspondence: jianqingmi@shsmu.edu.cn; sjchen@stn.sh.cn; heaili@xjtu.edu.cn

[1] Department of Hematology, The Second Affiliated Hospital of Xi'an Jiaotong University, 157 West 5th Road, Xi'an 710004, China
[5] State Key Laboratory of Medical Genomics, National Research Center for Translational Medicine, Shanghai Institute of Hematology, Ruijin Hospital Affiliated With Shanghai Jiao Tong University School of Medicine, 197 Ruijin er Road, Shanghai 200025, China
Full list of author information is available at the end of the article

Longest follow up of CAR-T therapy in RRMM to date

Zhao et al, Journal of Hematology & Oncology. 2022;15(86).

LEGEND-2: 4-year follow-up efficacy

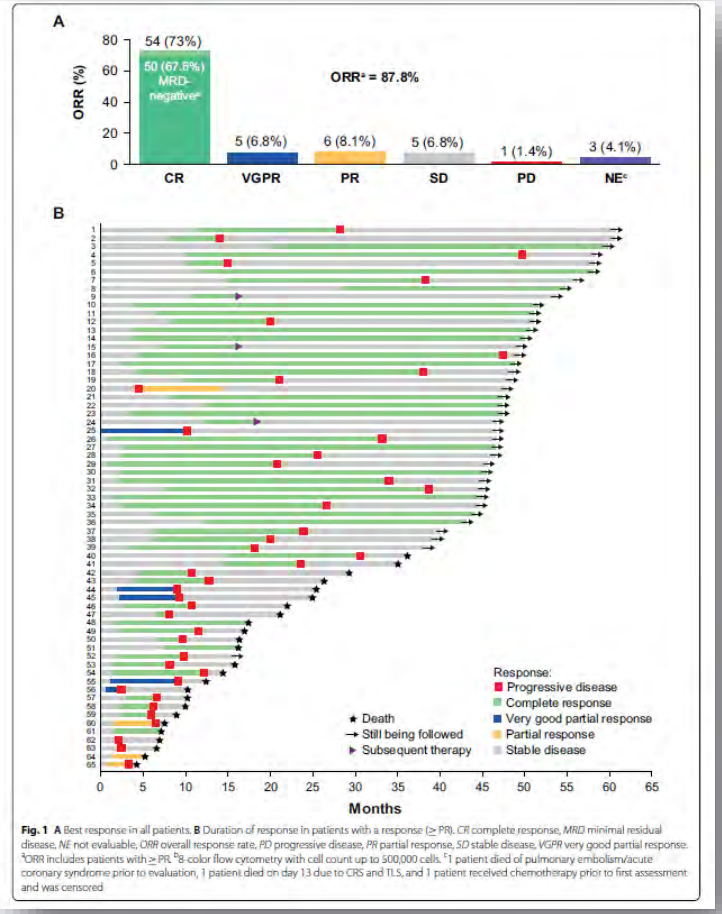


Fig. 1 **A** Best response in all patients. **B** Duration of response in patients with a response (≥ PR). *CR* complete response, *MRD* minimal residual disease, *NE* not evaluable, *ORR* overall response rate, *PD* progressive disease, *PR* partial response, *SD* stable disease, *VGPR* very good partial response. [a]ORR includes patients with ≥ PR. [b]8-color flow cytometry with cell count up to 500,000 cells. [c]1 patient died of pulmonary embolism/acute coronary syndrome prior to evaluation, 1 patient died on day 13 due to CRS and TLS, and 1 patient received chemotherapy prior to first assessment and was censored

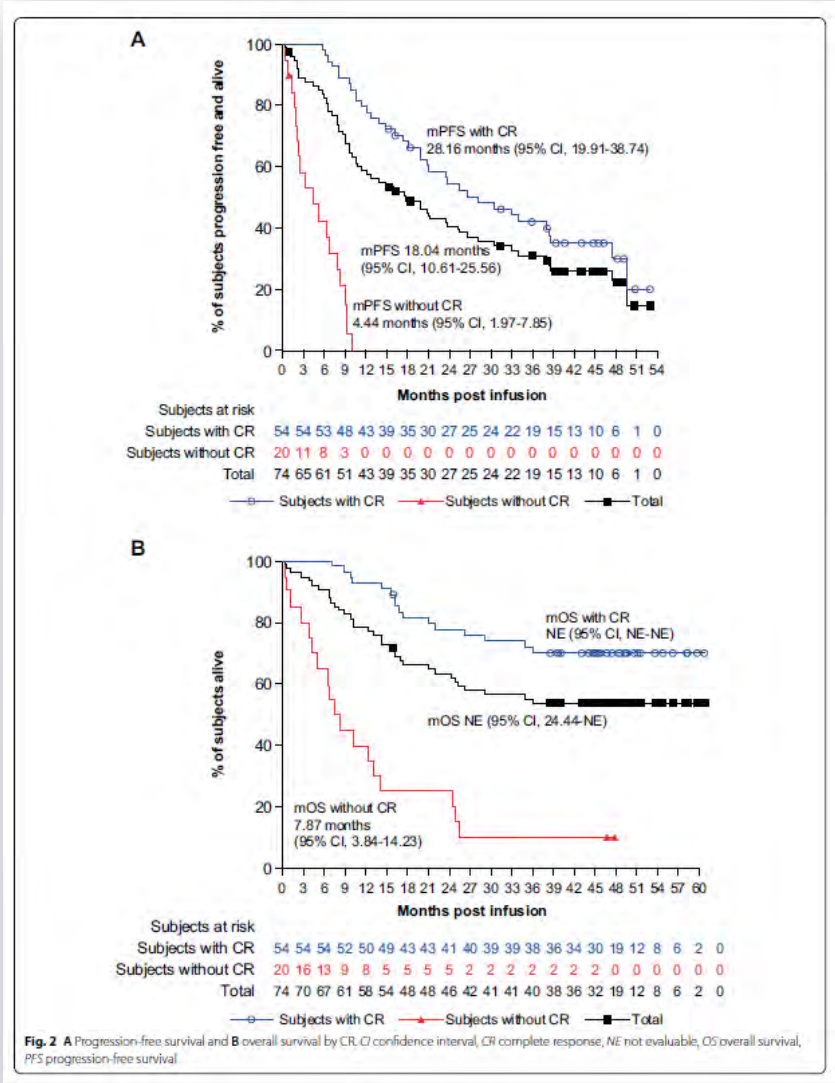


Fig. 2 **A** Progression-free survival and **B** overall survival by CR. *CI* confidence interval, *CR* complete response, *NE* not evaluable, *OS* overall survival, *PFS* progression-free survival

Zhao et al, Journal of Hematology & Oncology. 2022;15(86).

Global Clinical Development Plan

Ciltacabtagene autoleucel (cilta-cel)

CARTITUDE-1
Phase 1b/2, registrational (ASCO 2022 Update, JCO publication)

CARTITUDE-4
Phase III, 1-3 prior lines MM

CARTITUDE-6
Phase III, Newly diagnosed, transplant eligible

CARTITUDE-2
Phase II, Multi-cohort study in various MM settings (ASCO, IMS 2022)

CARTITUDE-5
Phase III, Newly diagnosed, transplant not intended/eligible

CARTITUDE-1

2 years post last patient in (~28-month follow up)

2022 ASCO, EHA, JCO

Journal of Clinical Oncology®

Original Reports

Ciltacabtagene Autoleucel, an Anti–B-cell Maturation Antigen Chimeric Antigen Receptor T-Cell Therapy, for Relapsed/Refractory Multiple Myeloma: CARTITUDE-1 2-Year Follow-Up

Thomas Martin, MD[1]; Saad Z. Usmani, MD[2]; Jesus G. Berdeja, MD[3]; Mounzer Agha, MD[4]; Adam D. Cohen, MD[5]; Parameswaran Hari, MD[6]; David Avigan, MD[7]; Abhinav Deol, MD[8]; Myo Htut, MD[9]; Alexander Lesokhin, MD[2]; Nikhil C. Munshi, MD[10,11]; Elizabeth O'Donnell, MD[12]; A. Keith Stewart, MBChB[13]; Jordan M. Schecter, MD[14]; Jenna D. Goldberg, MD[14]; Carolyn C. Jackson, MD, MPH[14]; Tzu-Min Yoh, MS[14]; Arnab Banerjee, MD[15]; Alicia Allred, PhD[15]; Enrique Zudaire, PhD[15]; William Deraedt, MSc[15]; Yunsi Olyslager, MSc[15]; Changwei Zhou, PhD[17]; Lida Pacaud, MD[17]; Deepu Madduri, MD[14]; Andrzej Jakubowiak, MD[18]; Yi Lin, MD, PhD[13]; and Sundar Jagannath, MD[2]

PURPOSE CARTITUDE-1, a phase Ib/II study evaluating the safety and efficacy of ciltacabtagene autoleucel (cilta-cel) in heavily pretreated patients with relapsed/refractory multiple myeloma, yielded early, deep, and durable responses at 12 months. Here, we present updated results 2 years after last patient in (median follow-up [MFU] approximately 28 months), including analyses of high-risk patient subgroups.

METHODS Eligible patients had relapsed/refractory multiple myeloma, had received ≥ 3 prior lines of therapy or were double refractory to a proteasome inhibitor and immunomodulatory drug and had received prior proteasome inhibitor, immunomodulatory drug, and anti-CD38 therapy. Patients received a single cilta-cel infusion 5-7 days after lymphodepletion. Responses were assessed by an independent review committee.

RESULTS At a MFU of 27.7 months (N = 97), the overall response rate was 97.9% (95% CI, 92.7 to 99.7); 82.5% (95% CI, 73.4 to 89.4) of patients achieved a stringent complete response. Median duration of response was not estimable. Median progression-free survival (PFS) and overall survival (OS) were not reached; 27-month PFS and OS rates were 54.9% (95% CI, 44.0 to 64.6) and 70.4% (95% CI, 60.1 to 78.6), respectively. Overall response rates were high across all subgroups (95.1%-100%). Duration of response, PFS, and/or OS were shorter in high-risk cytogenetic, International Staging System stage III, high tumor burden, and presence of plasmacytomas. The safety profile was manageable with no new cilta-cel–related cytokine release syndrome and one new case of Parkinsonism (day 914 after cilta-cel) since the last report.

CONCLUSION At approximately 28-month MFU, patients treated with cilta-cel maintained deep and durable responses, observed in both standard and high-risk subgroups. The risk/benefit profile of cilta-cel remained favorable with longer follow-up.

J Clin Oncol 00. © 2022 by American Society of Clinical Oncology

INTRODUCTION

The standard of care (SOC) for relapsed multiple myeloma (MM) involves a multidrug regimen that may include a proteasome inhibitor (PI), an immunomodulatory drug (IMiD), a monoclonal antibody, and a corticosteroid.[1] However, patients may eventually become resistant to these treatments.[2,3] Lower depth and durability of response have been reported with each successive line of therapy (LOT),[4] and patients who are refractory to multiple drug classes have suboptimal outcomes. The median overall survival (OS) with SOC is 11.2 months for patients who are refractory to <3 prior LOT and 5.6 months for penta-refractory patients (refractory to anti-CD38 antibody, two PIs, and two IMiDs).[2]

There is an unmet medical need to extend survival and delay progression in heavily pretreated patients with refractory MM. Two novel agents with different mechanisms of action, selinexor[5] and belantamab mafodotin,[6] were recently approved for patients with relapsed or refractory MM (RRMM) who received ≥ 4 prior LOT but had overall response rates (ORRs) of only 21% to 34% in clinical trials.[7,8]

Personalized immunotherapy using a chimeric antigen receptor (CAR) involves genetically modifying a patient's own T cells so that they can identify and kill malignant plasma cells.[9,10] The first B-cell maturation antigen (BCMA)–directed CAR-T cell immunotherapy, idecabtagene vicleucel (ide-cel), was approved in the

ASSOCIATED CONTENT
Appendix
Protocol
Author affiliations and support information (if applicable)
Accepted on May 6, 2022 and published at ascopubs.org/journal/jco on XX XX, 2022: DOI: https://doi.org/10.1200/JCO.22.00842

ASCO

Journal of Clinical Oncology

At a median follow-up of 28 months, patients treated with cilta-cel maintained deep and durable responses, with median PFS and OS not yet reached, and a manageable safety profile

- The ORR to cilta-cel remained at 98%, with 83% of patients achieving sCR with longer follow-up
- The safety profile was manageable with a favorable risk-benefit profile and one new case of parkinsonism (day 914 after cilta-cel) since the last report
- Cilta-cel is currently under further investigation in patients with MM in earlier-line settings in CARTITUDE-2, CARTITUDE-4, CARTITUDE-5, EMagine/CARTITUDE-6[1]

SCAN ME

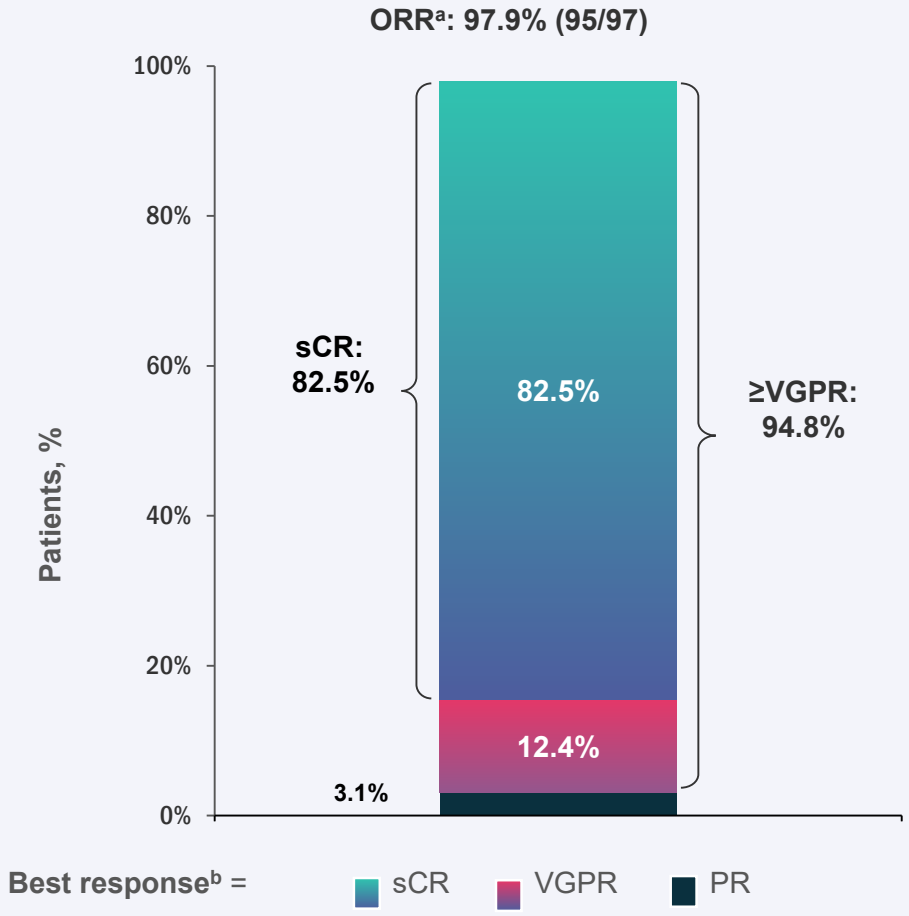
ascopubs.org/doi/full/10.1200/JCO.22.00842

Martin et al. *J Clin Oncol*. 2022. doi: 10.1200/JCO.22.00842; Usmani et al. ASCO Annual Meeting; June 3-7, 2022; Chicago, Il & Virtual; Abstract #8028

1. ClinicalTrials.gov: CARTITUDE-2 (NCT04133636); CARTITUDE-4 (NCT04181827); CARTITUDE-5 (NCT04923893); EMagine/CARTITUDE-6 EMN28 (NCT05257083).

LEGEND BIOTECH

CARTITUDE-1: Median PFS and OS not reached at median follow up of 27.7 months



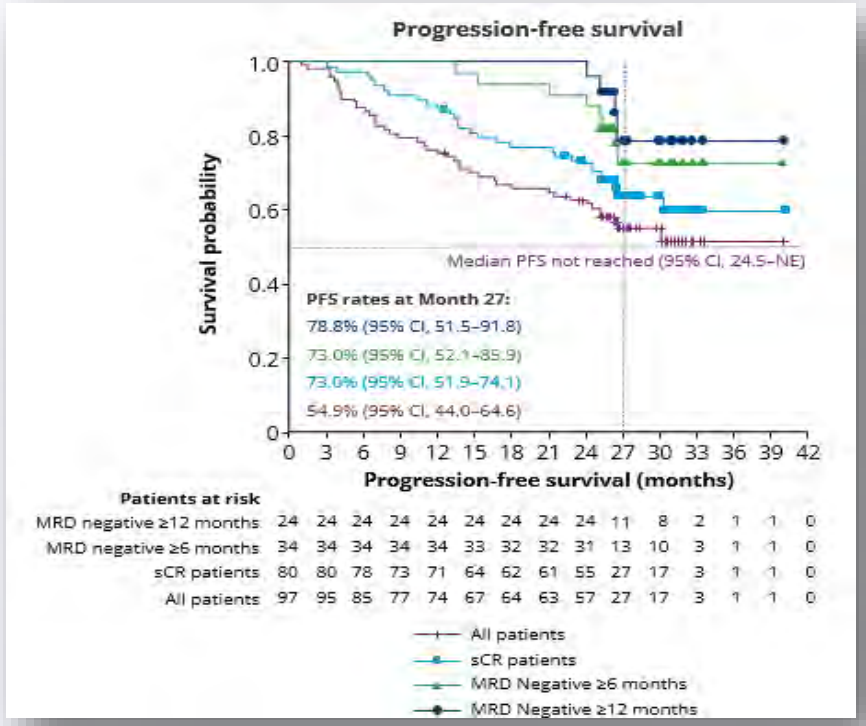
Responses deepened over time from the 12-month follow-up

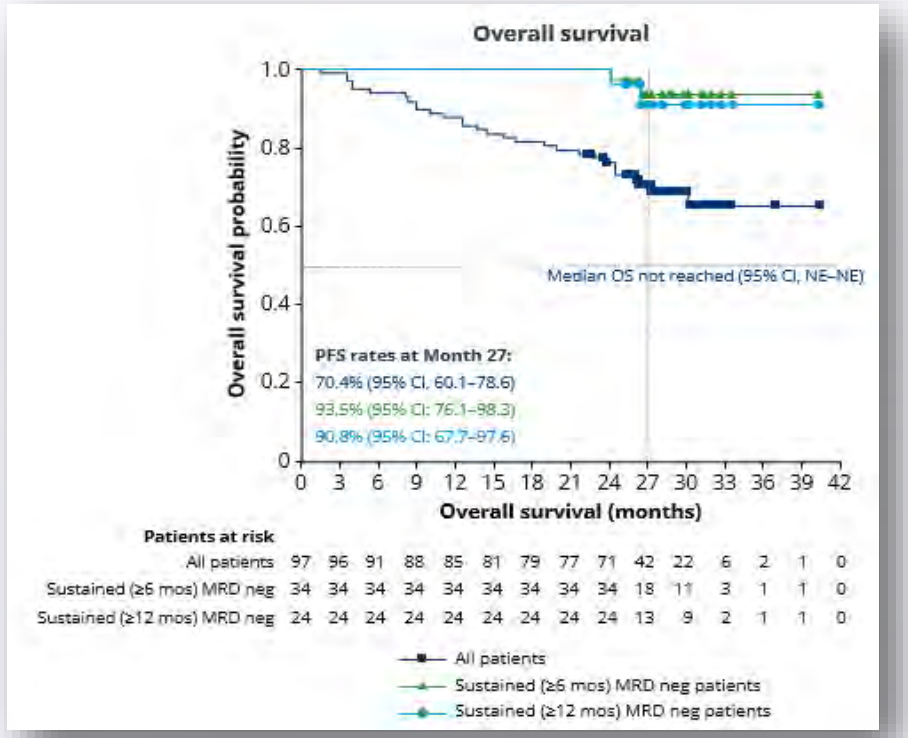
- Most patients in high-risk subgroups responded (ORR range 95.1–100%), including those with high-risk cytogenetics, high tumor burden, or baseline plasmacytomas
  - DOR, PFS, and/or OS were shorter in subgroups with high-risk cytogenetics, ISS stage III, high tumor burden, or plasmacytoma
- High ORR was achieved despite a lack of detectable CAR-T cell persistence over time

Data cut-off: January 11, 2022; aORR assessed by independent review committee. bNo patient had CR or stable disease. CAR, chimeric antigen receptor; DOR, duration of response; ISS, International Staging System; MRD, minimal residual disease;
NE, not estimable; ORR, overall response rate; OS, overall survival; PR, partial response; PFS, progression-free survival; sCR, stringent CR; VGPR, very good partial response

Usmani et al. ASCO Annual Meeting; June 3-7, 2022; Chicago, Il & Virtual; Abstract #8028; Martin et al. J Clin Oncol. 2022. doi: 10.1200/JCO.22.00842

CARTITUDE-1: Median PFS and OS not reached at median follow up of 27.7 months





- Median PFS and OS were not reached with median follow up of 27.7 months
- Patients who achieved sCR had improved PFS compared with the overall population
- Of 61 patients evaluable for MRD, 91.8% were MRD-negative at (10^{-5})
- Patients with sustained MRD negativity (10^{-5}) for ≥6 and ≥12 months had improved PFS and OS compared with the overall population

Data cut-off: January 11, 2022; MRD, minimal residual disease; OS, overall survival; PFS, progression-free survival; sCR, stringent CR

Usmani et al. ASCO Annual Meeting; June 3-7, 2022; Chicago, Il & Virtual; Abstract #8028; Martin et al. J Clin Oncol. 2022. doi: 10.1200/JCO.22.00842

CARTITUDE-1: Safety (median follow up of 27.7 months)

The safety profile was manageable with no new treatment-related deaths

- A total of 20 SPMs were reported in 16 patients, none were classified as related to cilta-cel.
  - 9 patients with hematologic malignancies (1 low-grade B-cell lymphoma, 6 MDS, 3 fatal AML*)
  - 1 patient each with malignant melanoma, adenocarcinoma, myxofibrosarcoma, and prostate cancer
  - 6 non-melanoma skin cancers

  This patient population was heavily pretreated, including IMiDs (100%), alkylating agents (melphalan 83%, cyclophosphamide 65%) and/or autologous stem-cell transplantation, all of which are associated with increased risk of SPM.
- One new case of signs and symptoms of parkinsonism on Day 914
  - On day 914, patient experienced cognitive slowing, gait instability, and neuropathy (all grade 1), and tremor (grade 3); he is currently stable and functioning and remains in sCR
- Following implementation of patient management strategies, the incidence of movement and neurocognitive disorders (parkinsonism) has decreased from 6% in CARTITUDE-1 to <0.5% across the CARTITUDE program

* One patient had both MDS and fatal AML

Usmani et al. ASCO Annual Meeting; June 3-7, 2022; Chicago, Il & Virtual; Abstract #8028; Martin et al. *J Clin Oncol*. 2022. doi: 10.1200/JCO.22.00842

CARTITUDE-1

RRMM: PI, IMiD and anti-CD38 exposed

- 2022 CARVYKTI approvals, indications and market opportunity
  - US Approval: February 28
    - Indication: 5L+ Prior lines of therapy
    - Patient opportunity: ~12,000
  - EU Conditional Approval: May 25
    - Indication: 4L+ Prior lines of therapy
    - Patient opportunity: ~6,000
  - Japan Approval: Approved September 26
    - Indication: 4L+ Prior lines of therapy
    - Patient opportunity: ~4,000

Opportunity Assessment

*Estimate includes patients eligible for lead indication; Lead indication label
US label aligns with FDA approved label 2/28/2022
EU label indicates patients who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody and have demonstrated disease progression on the last therapy
JP label assumption aligns with the EU label
Source: Kantar Health, Precision-IQ, SHS/Komodo Claims

CARTITUDE-1

RRMM: PI, IMiD and anti-CD38 exposed

- CARVYKTI go to market model
  - US
    - 50/50 co-commercialize with Janssen
    - Legend deployment is largely hospital based
    - Implementing phased approach
  - Rest of World
    - Janssen leads commercial activities outside of US, with exception of China
- Product Positioning
  - Clinical
  - Operationally
  - Access

Opportunity Assessment

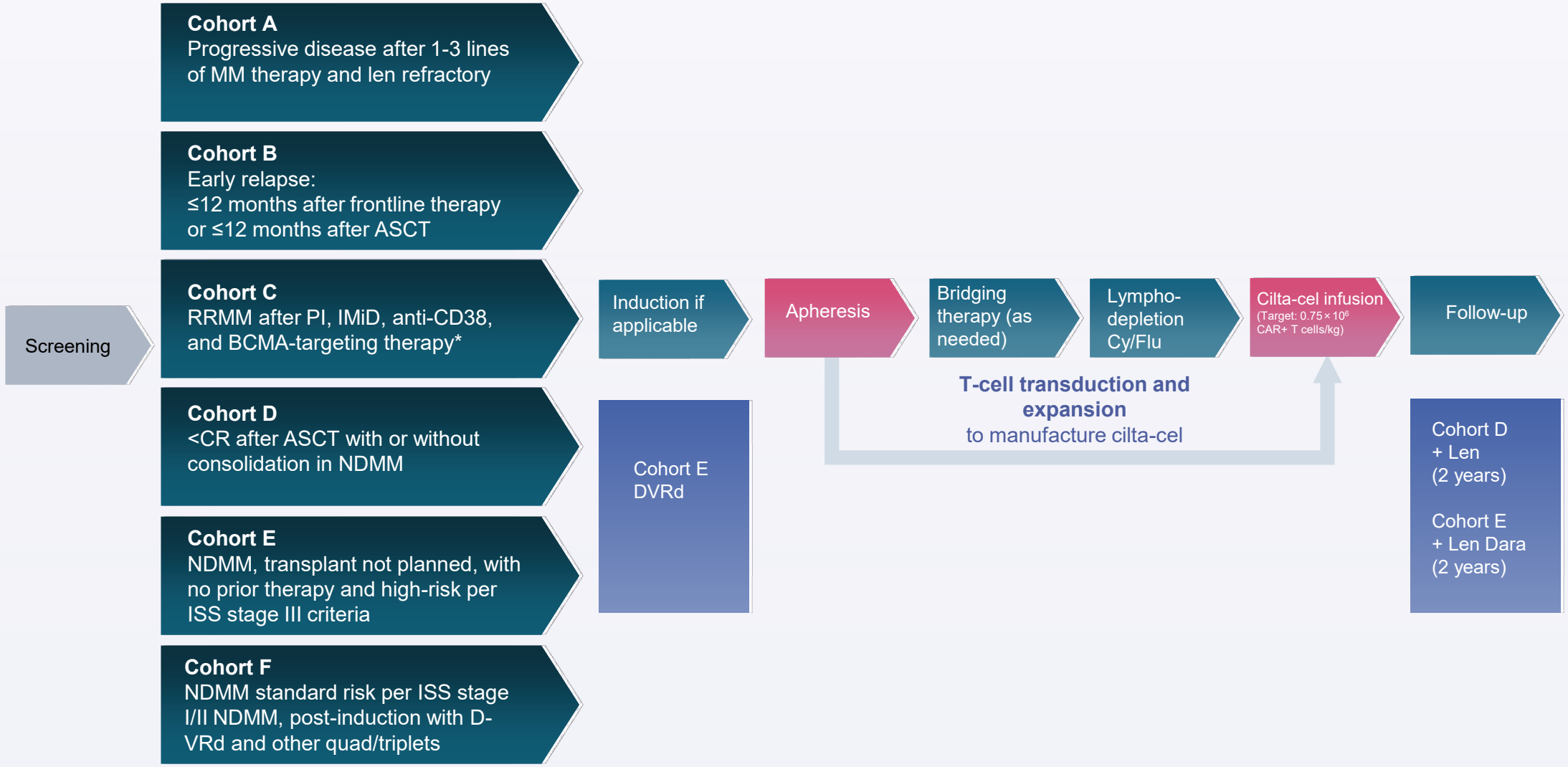
*Estimate includes patients eligible for lead indication; Lead indication label
US label aligns with FDA approved label 2/28/2022
EU label indicates patients who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody and have demonstrated disease progression on the last therapy
JP label assumption aligns with the EU label
Source: Kantar Health, Precision-IQ, SHS/Komodo Claims

CARTITUDE-2 Cohort C:

Progressive MM after treatment with prior BCMA-targeting therapy

2022 IMS and *Blood*

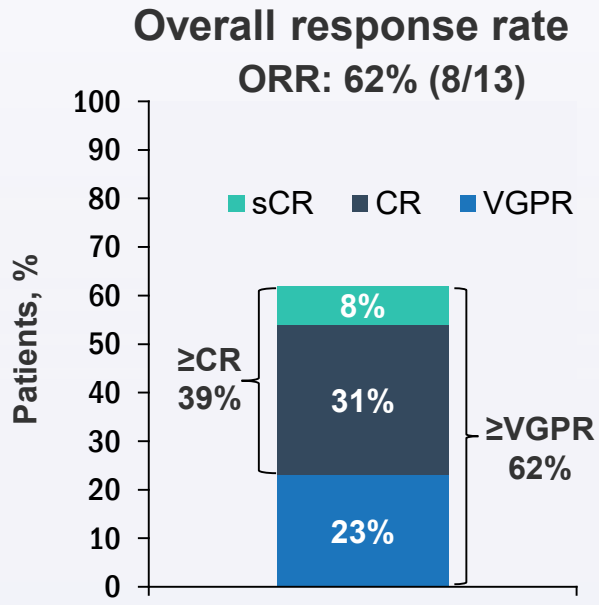
CARTITUDE-2: Phase II Multi-Cohort Study in Various Multiple Myeloma Settings (n ≈ 160)



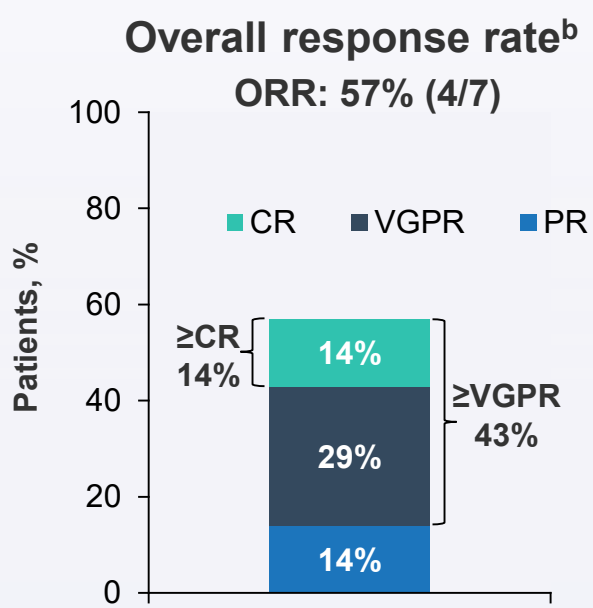
DVRd, Darzalex, Velcade, Revlimid, dexamethasone; IMiD, immunomodulatory drugs; NDMM, newly diagnosed multiple myeloma; RRMM, relapse refractory multiple myeloma; ASCT, autologous stem cell transplant; ISS, International Staging System *Excluding prior BCMA-targeting cellular therapy

CARTITUDE-2 Cohort C: Efficacy Response

Prior ADC



Prior BsAb



- Median follow-up of 11.3 months
- 80% of patients were refractory to prior anti BCMA therapy
- For patients who received prior ADC therapy (n=13), ORR was 62%
- For patients who received prior BsAb therapy (n=7), ORR was 57%
- Median time to first response was ~ 1 month

Data cutoff: October 8, 2021; [a]Evaluable samples are those that pass calibration and QC and include sufficient cells for evaluation at 10^{-5} threshold. [B]2 patients died before confirmed response
ADC, antibody-drug conjugate; CR, complete response; MRD, minimal residual disease; ORR, overall response rate; sCR, stringent complete response; VGPR, very good partial response.

Cohen et al. 19th IMS Annual Meeting; Aug 25-27, 2022; Los Angeles, CA; Cohen AD, et al. Blood 2022.

CARTITUDE-2 Cohort C: Safety

- Overall, CRS occurred in 12 patients
  - Median time to onset was 7.5 days (range, 2–10)
  - Median duration was 7 days (range, 2–9)
  - All patients who had CRS received ≥1 treatment for it
- 4 patients had ICANS
  - Median time to onset was 9.0 days (range, 4–13)
  - Median duration was 7.0 days (range, 4–20)
  - ICANS resolved in 3 patients[a]
  - ICANS in cohort C overall (20%) was comparable to that in CARTITUDE-1[1] (17%)
- No cases of MNTs/parkinsonism were observed in this cohort
- 7 deaths occurred in cohort C (1 due to treatment related AE, 3 due to unrelated AE, 3 due to progressive disease)

- Patients were more heavily pre-treated than those in CARTITUDE-1, but safety profile remained consistent
- Cilta-cel induced favorable benefit/risk in heavily pre-treated (~80% prior BCMA refractory) MM patients with prior anti-BCMA exposure

[a] For the case that did not resolve, the patient had several other severe conditions, including *C difficile* colitis, kidney failure, respiratory failure, and hemophagocytic lymphohistiocytosis. This patient died on study day 17 from *C difficile* colitis.

[1] Berdeja J, et al. *Lancet* 2021; 398:314-24.

AE, adverse event; ADC, antibody-drug conjugate; CRS, cytokine release syndrome; ICANS, immune effector cell–associated syndrome; MNT, movement and neurocognitive treatment-emergent adverse event.

Cohen et al. 19th IMS Annual Meeting; Aug 25-27, 2022; Los Angeles, CA; Cohen AD, et al. Blood 2022.

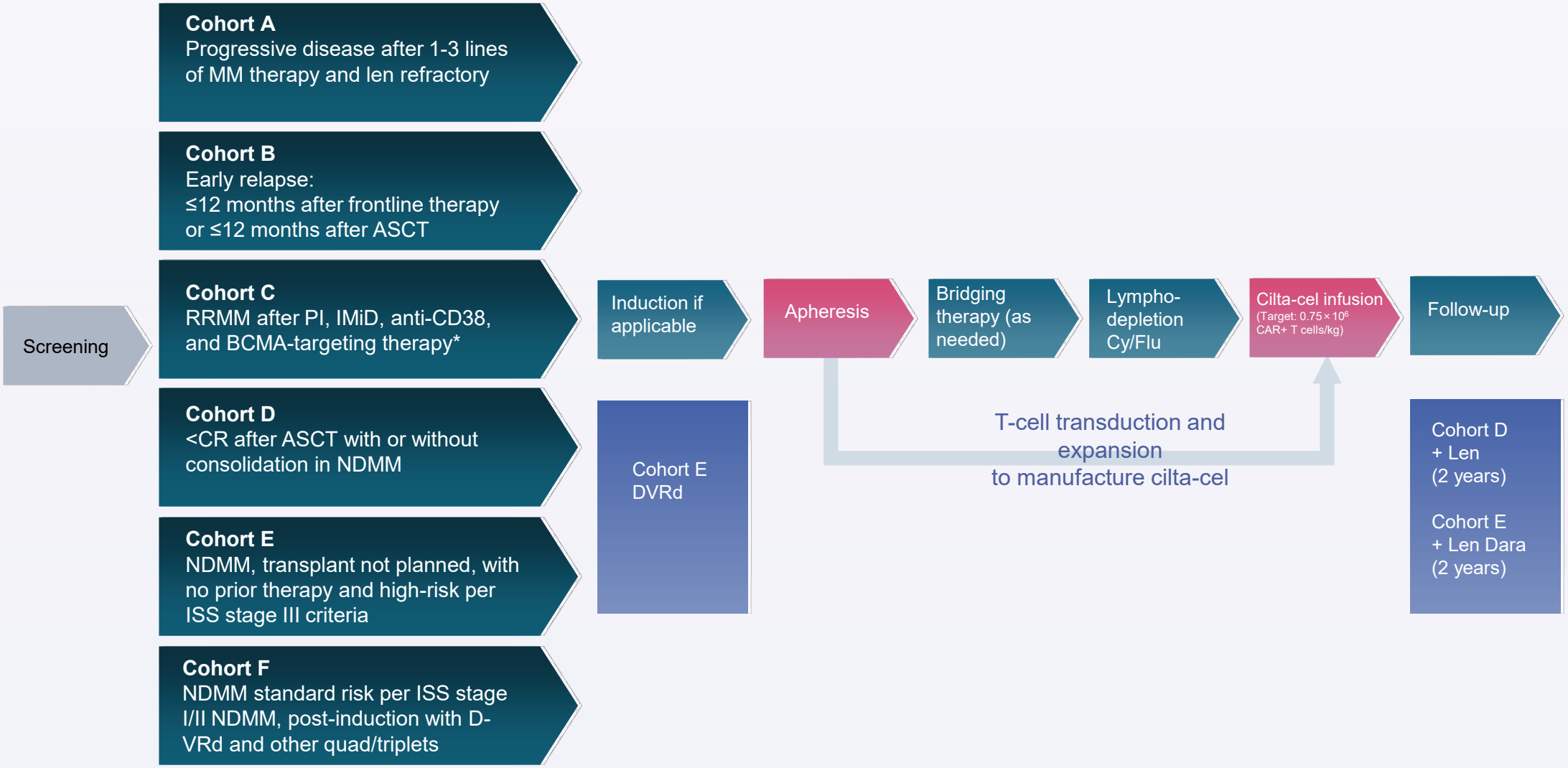
RRMM after 1–3 prior lines of therapy

CARTITUDE-2 Cohort A: Progressive MM after 1–3 prior lines of therapy and lenalidomide refractory

CARTITUDE-2 Cohort B: Early relapse MM within 12 months after initial therapy

CARTITUDE-4: Phase 3 ongoing study

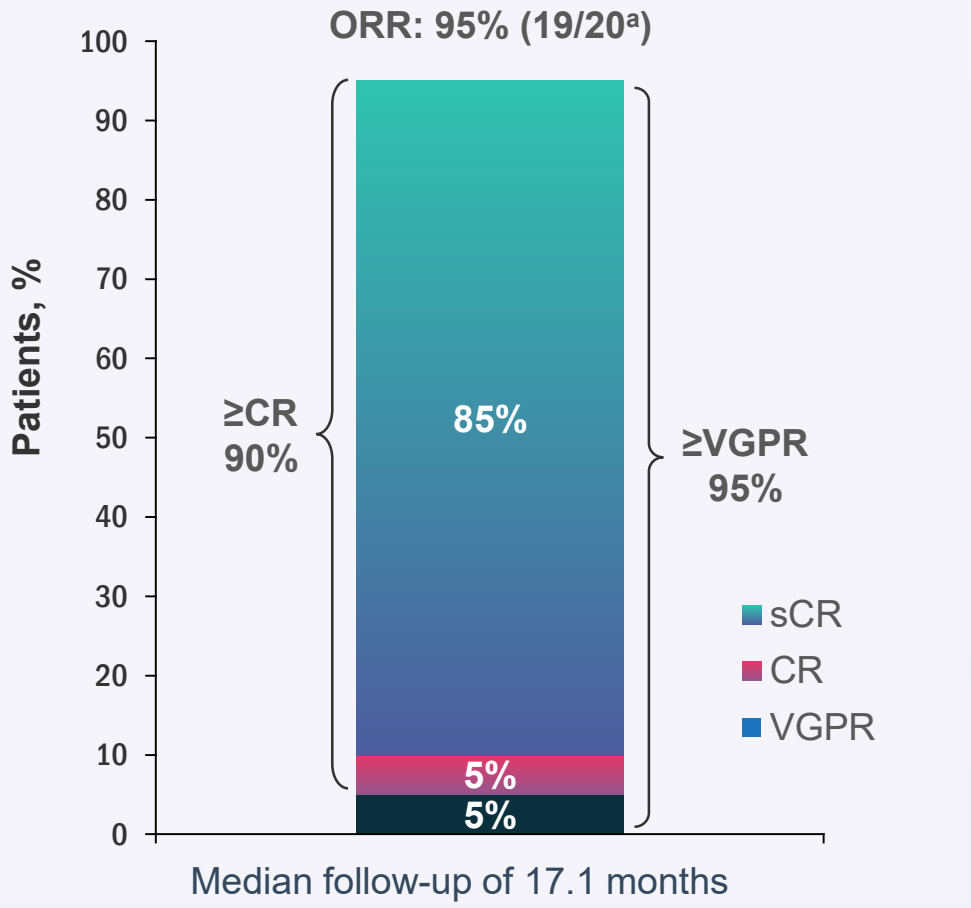
CARTITUDE-2: Phase II Multi-Cohort Study in Various Multiple Myeloma Settings (n ≈ 160)



DVRd, Darzalex, Velcade, Revlimid, dexamethasone; IMiD, immunomodulatory drugs; NDMM, newly diagnosed multiple myeloma; RRMM, relapse refractory multiple myeloma; ASCT, autologous stem cell transplant; ISS, International Staging System; *Excluding prior BCMA-targeting cellular therapy

CARTITUDE-2 Cohort A (N=20)

Progressive MM After 1–3 Prior Lines of Therapy and Lenalidomide Refractory



Responses to cilta-cel deepened over time

- Median DOR was not reached
- Median time to first response:1.0 month (range, 0.7–3.3)
- Median time to best response: 2.6 months (range, 0.9–13.6)
- 15-month PFS rate was 70% (95% CI, 45.1–85.3)
- All 16 patients with evaluable samples were MRD negative at 10^{-5}

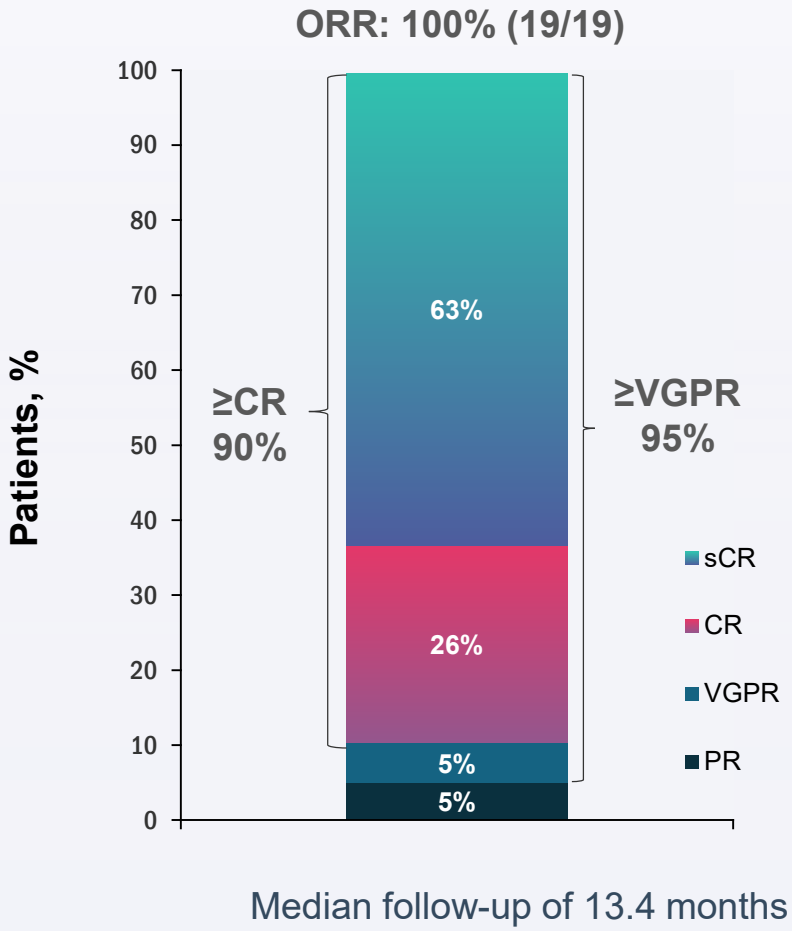
Safety:

- Safety was manageable including the 1 patient treated in outpatient setting
- CRS: All grade: 95%; ≥ Grade 3: 10%
- Neurotoxicity: All grade: 30%; Grade 3/4: 5%
  - No cases of MNTs/signs and symptoms of parkinsonism
- 4 deaths occurred: 2 due to PD (days 426 and 550), 1 due to sepsis (not treatment related, day 394), 1 death due to COVID-19 (treatment related, day 100)

January 2022 data cutoff; [a]1 patient demonstrated a minimal response.
CR, complete response; MRD, minimal residual disease; ORR, overall response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; sCR, stringent complete response; VGPR, very good partial response
Einsele et al. ASCO Annual Meeting; June 3-7, 2022; Chicago, Il & Virtual; Abstract #8020

CARTITUDE-2 Cohort B (N=19)

Early relapse within 12 months after initial therapy including PI and IMiD



Median follow-up of 13.4 months

Responses to cilta-cel deepened over time

- Median DOR was not reached
- Median time to first response:1.0 month (range, 0.9-9.7)
- Median time to best response: 5.1 months (range, 0.9–11.8)
- 12-month PFS rate was 89.5% (95% CI, 64.1–97.3)
- Of the 15 patients with MRD evaluable samples at the 10^{-5} threshold, 93% were MRD negative

Safety:

- Safety was manageable including the 1 patient treated in an outpatient setting
- CRS: All grade: 84%; Grade 3/4: 5%
- Neurotoxicity: All grade: 26%; Grade 3/4: 5%
  - 1 patient with MNT/signs and symptoms of parkinsonism
- 1 death due to progressive disease (day 158)

January 2022 data cut-off.
AE, adverse event; CAR, chimeric antigen receptor; CR, complete response; CRS, cytokine release syndrome; ICANS, immune effector cell–associated neurotoxicity; MNT, movement and neurocognitive treatment-related adverse event; MRD, minimal residual disease; ORR, overall response rate; PFS, progression-free survival; PR, partial response; sCR, stringent complete response; VGPR, very good partial response
Van de Donk et al. ASCO Annual Meeting; June 3-7, 2022; Chicago, Il & Virtual; Abstract #8029

Summary: Relapsed or refractory MM datasets

Consistent efficacy results across 3 datasets with a manageable safety profile

98% ORR
83% sCR
mPFS Not Reached at 27.7 mo follow-up

CARTITUDE-1[1]
(N=97)

≥3 prior therapies or double refractory, Prior PI, IMiD, anti-CD38 antibody exposure

95% ORR
90% sCR/CR
mPFS Not Reached at 17.1 mo follow-up

CARTITUDE-2
Cohort A[2]
(N=20)

Progressive MM After 1–3 Prior Lines of Therapy and Lenalidomide Refractory

100% ORR
90% sCR/CR
mPFS Not Reached at 13.4 mo follow-up

CARTITUDE-2
Cohort B[3]
(N=19)

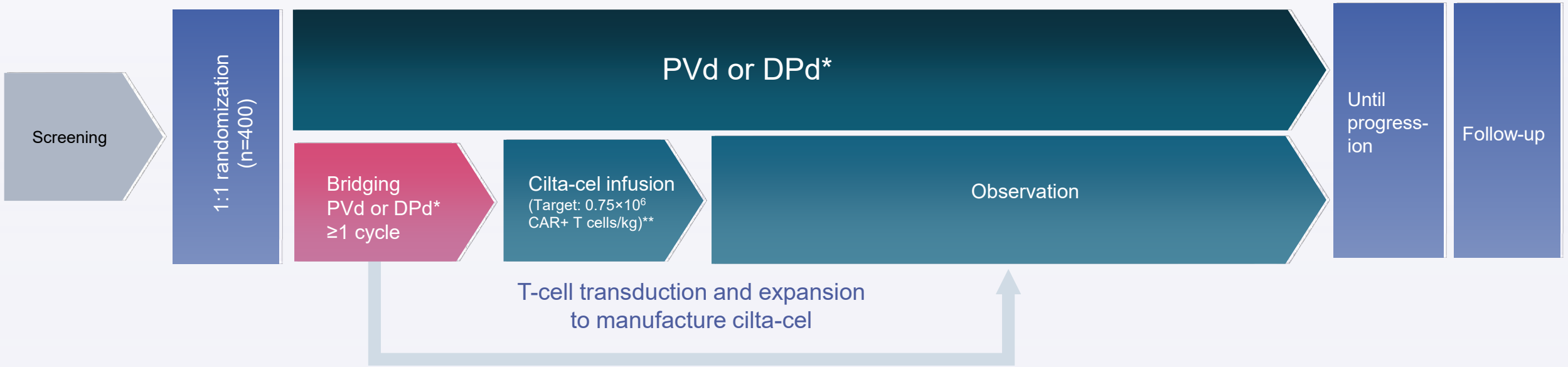
Early relapse after front-line therapy including PI, IMiD or ASCT

Ongoing Ph 3
CARTITUDE-4

After 1–3 Prior Lines of Therapy and Lenalidomide Refractory

1. Usmani et al. ASCO Annual Meeting; June 3-7, 2022; Chicago, Il & Virtual; Abstract #8028; 2. Einsele et al. ASCO Annual Meeting; June 3-7, 2022; Chicago, Il & Virtual; Abstract #8020; 3. Van de Donk et al. ASCO Annual Meeting; June 3-7, 2022; Chicago, Il & Virtual; Abstract #8029

CARTITUDE-4: Phase III Study in 1-3 prior line RRMM (NCT04181827)



KEY INCLUSION CRITERIA

- 1–3 prior lines of therapy (PI+IMiD or PI+IMiD+CD38 exposed), and lenalidomide-refractory
- No Prior CAR-T or BCMA-targeting therapy

STATUS

- Fully enrolled
- ~100 study locations, in 17 countries in North America, Europe and Asia.

PVd : Pomalyst, Velcade, dexamethasone. * Physician's choice and dependent on prior anti-myeloma therapy. ** Conditioning regimen: cyclophosphamide/ fludarabine. Study start/locations source: clinicatrials.gov

Myeloma RRMM Triplet Efficacy Outcomes--current SoC

Regimen	% Len Refractory	Median PFS (Months)	Median PFS for Len Refractory Patients (Months)	Median Lines of Therapy (Publication)	Study Name and Reference
PVd arm (n=281)	71% (PVd)	11.2	9.5	2	OPTIMISMM; Richardson 2019
DPd (n=103)	89%	8.8	8.8	4	EQUULEUS; Chari 2017
DPd (n=151)	80%	12.4	10	2	APOLLO; Dimopoulos 2022
DVd arm (n=251)	17.9% (DVd)	16.7	9.3	2	CASTOR; Spencer 2018

DVd: Darzalex, Velcade, dexamethasone
PVd : Pomalyst, Velcade, dexamethasone
DPd: Darzalex,, Pomalyst, dexamethasone

CARTITUDE-4

RRMM: 1-3 PL (PI+IMiD exposed + lenalidomide refractory)

First Phase 3 Global BCMA CAR-T cell therapy Clinical Trial in 1-3 prior line setting

Cilta-cel potential indication assumption

- 1-3 prior lines of therapy
  - Does not require prior daratumumab exposure
    - ~80% of patients in 2L setting have not been daratumumab exposed
    - *Eligible patient opportunity
      - US: ~36,000
      - EU: ~16,000
      - JP: ~5,000
  - Timing: TBD

Competitive assumption

- 2-4 Prior lines of therapy
  - Requires prior daratumumab exposure
  - Timing: 2H23

Opportunity Assessment

Source: Kantar Health, Precision-IQ, SHS/Komodo Claims

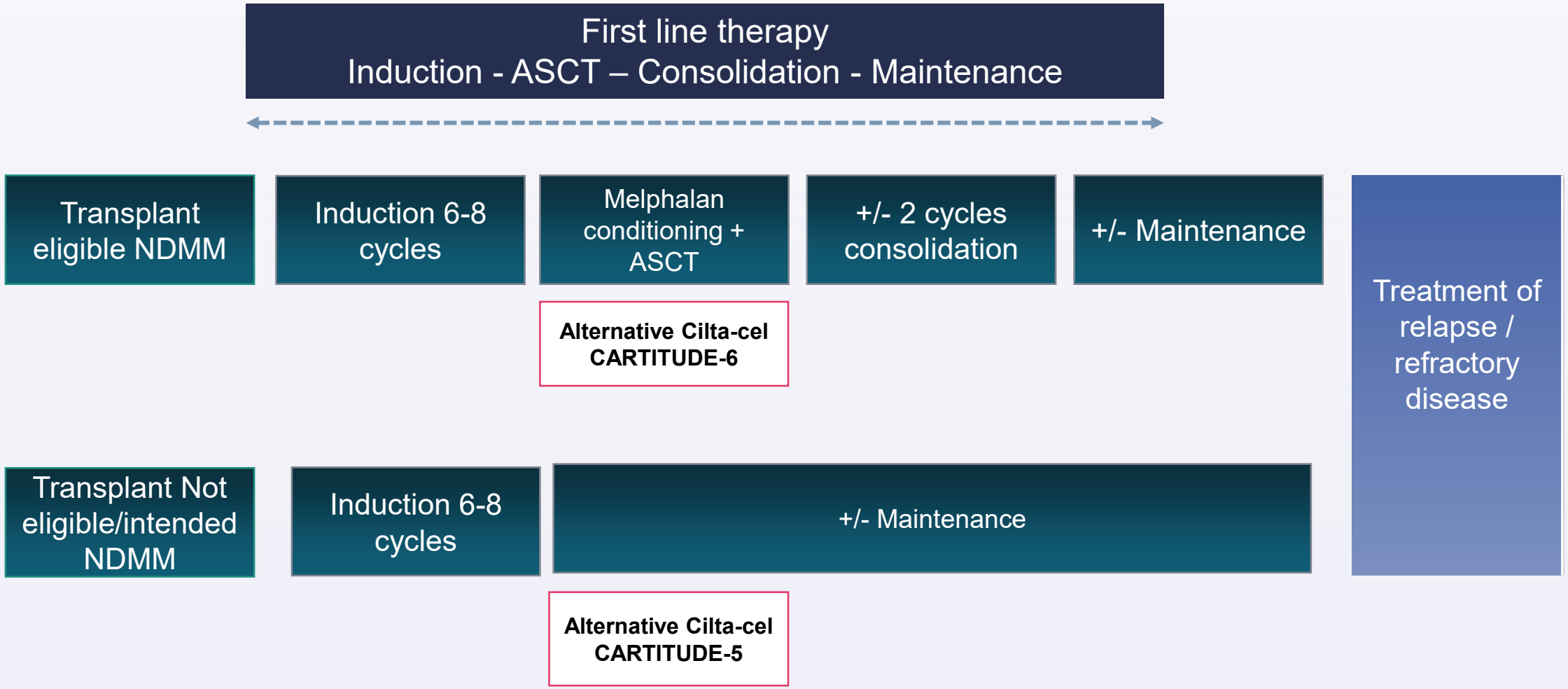
Newly Diagnosed MM

CARTITUDE-5: Ph 3, Newly Diagnosed MM, not intended/eligible for transplant

CARTITUDE-6: Ph 3, Newly diagnosed, transplant eligible

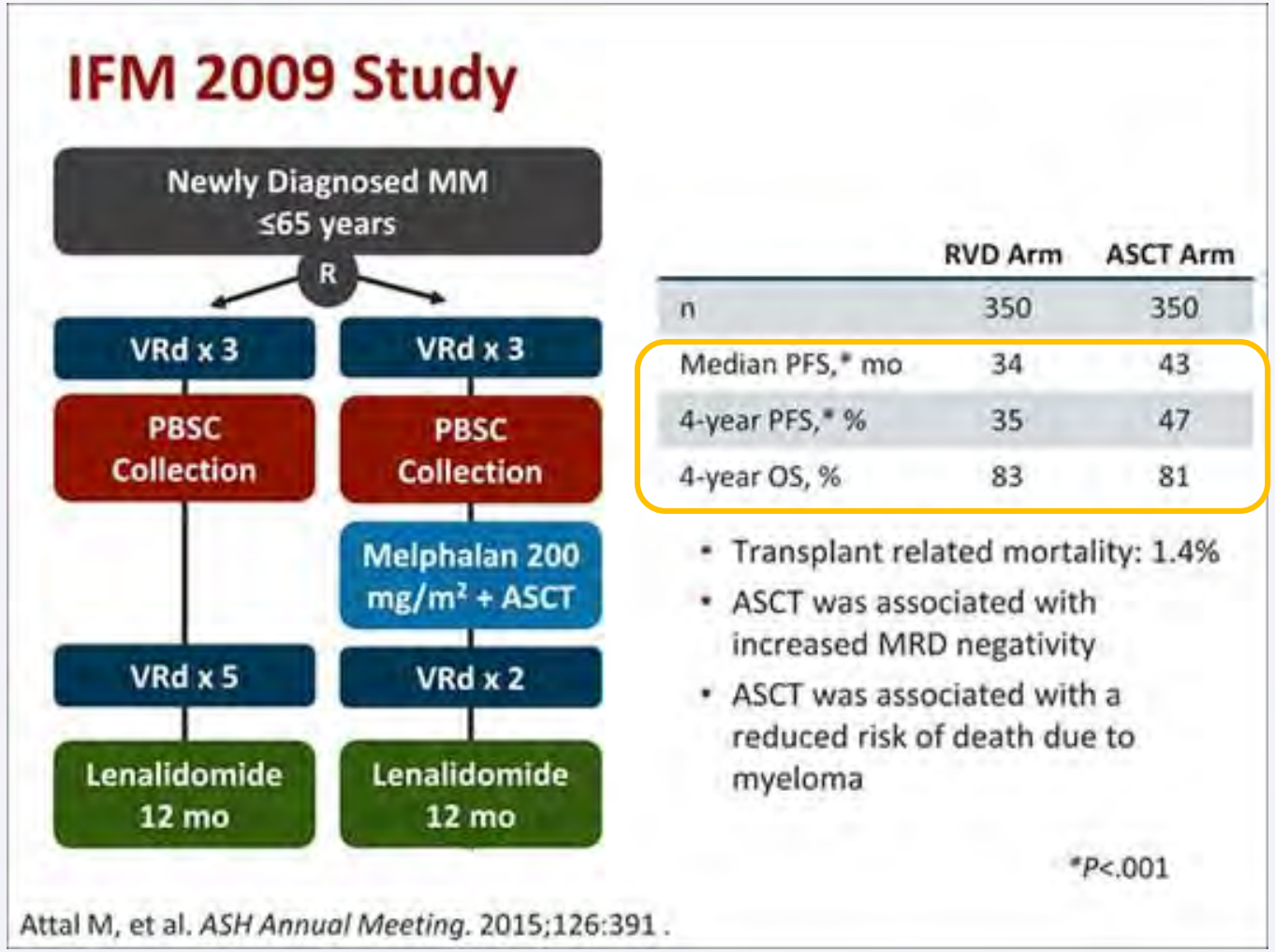
Newly Diagnosed MM (NDMM) Treatment Schema

Potential role of cilta-cel



ASCT – Autologous Stem Cell Transplant

Similar OS Outcome for Transplant: 1L or 2L



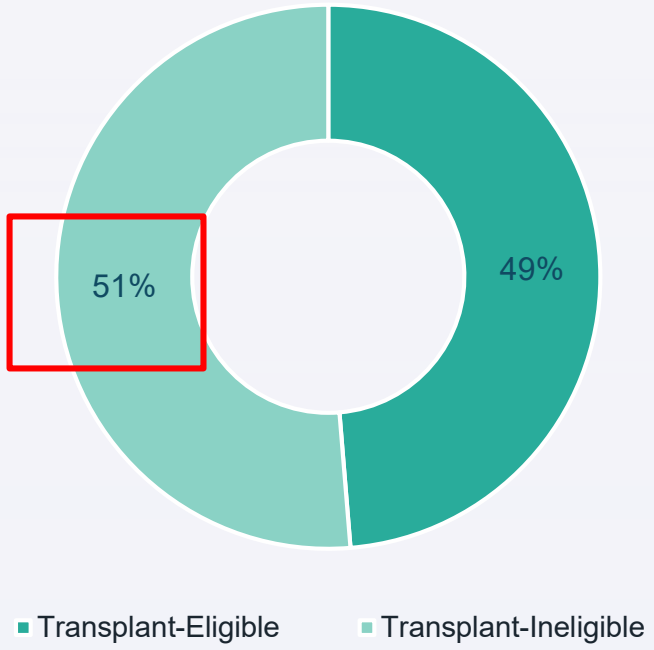
SWOG 0777 study (Durie BG, et al *Lancet.* 2017) **:** suggested that VRD alone has comparable PFS/OS to HDT/ASCT.

IFM2009 randomized study (Attal M, et al *N. Engl. J. Med.* 2017) :
Showed no overall survival (OS) benefit for participants who were randomized to VRd + early ASCT compared to participants who received VRd + deferred ASCT until after first relapse.

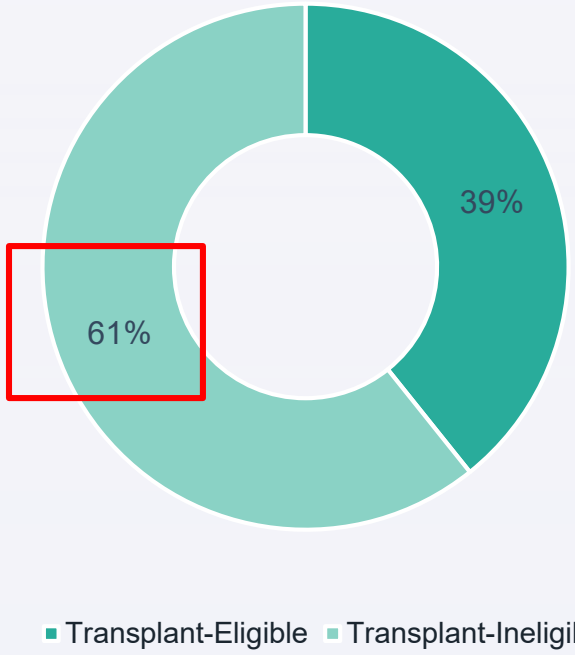
ASCT- Autologous Stem Cell Transplant

~51% (US) and ~61% (EU) of NDMM Patients are Ineligible for Transplant

Transplant Eligibility Among Newly-Diagnosed Patients, Multiple Myeloma, U.S., 2020*



Transplant Eligibility Among Newly Diagnosed Patients, Multiple Myeloma, EU5, 2020*

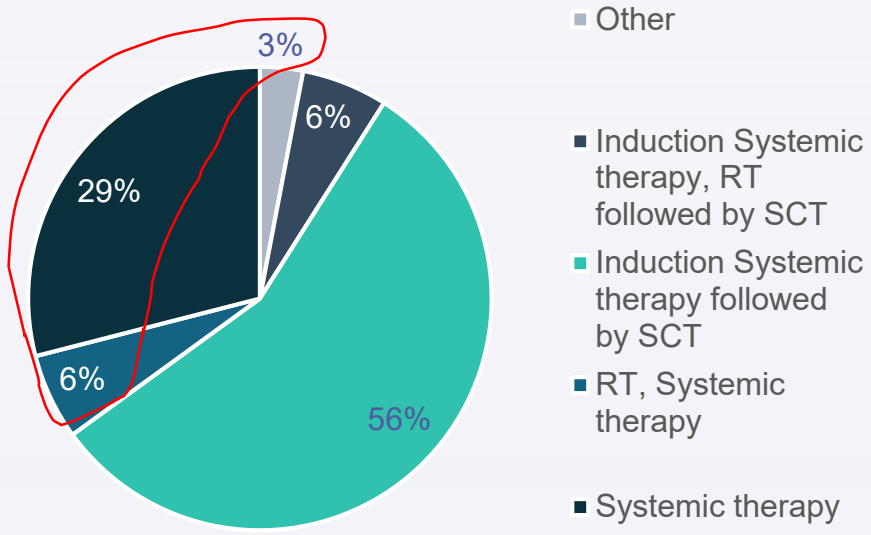


Source: CancerMPact Treatment Architecture, US and EU5, Multiple Myeloma; by Kantar, published 11/20

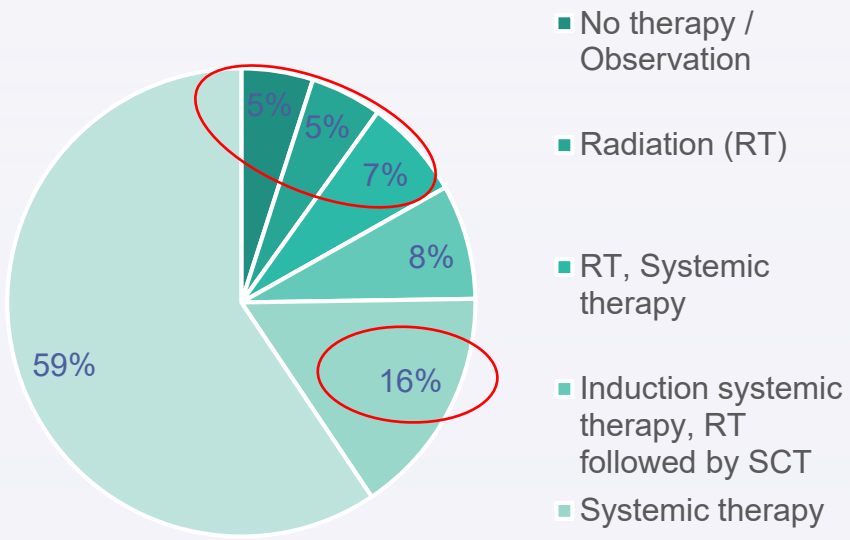
*QM7 (n=101): What percent of your newly-diagnosed multiple myeloma patients are transplant-eligible and what percent are transplant-ineligible?

~38% (US) and ~32% (EU) of NDMM patients are eligible for SCT, but do not receive it initially

Initial Treatment Modality Utilization for Transplant Eligible Patients, Multiple Myeloma, U.S., 2020*



Initial Treatment Modality Utilization for Transplant Eligible Patients, Multiple Myeloma, EU5, 2020*

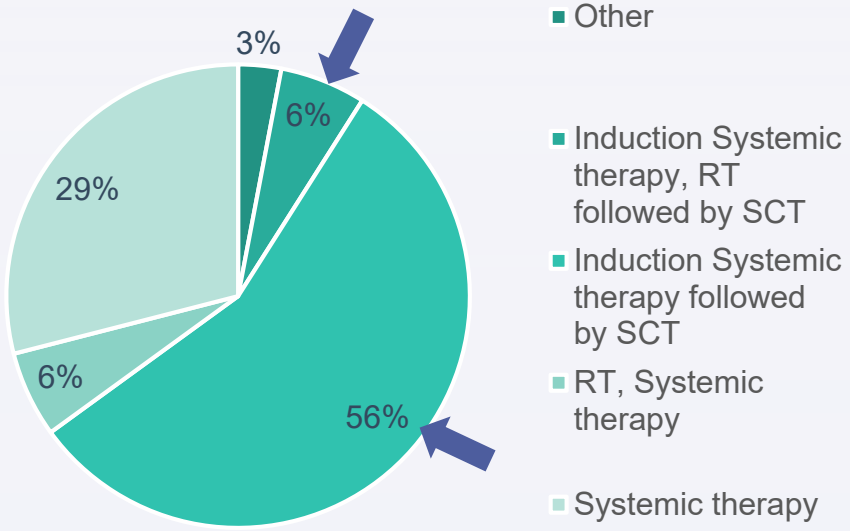


Source: CancerMPact Treatment Architecture, US and EU5, Multiple Myeloma; by Kantar, published 11/20

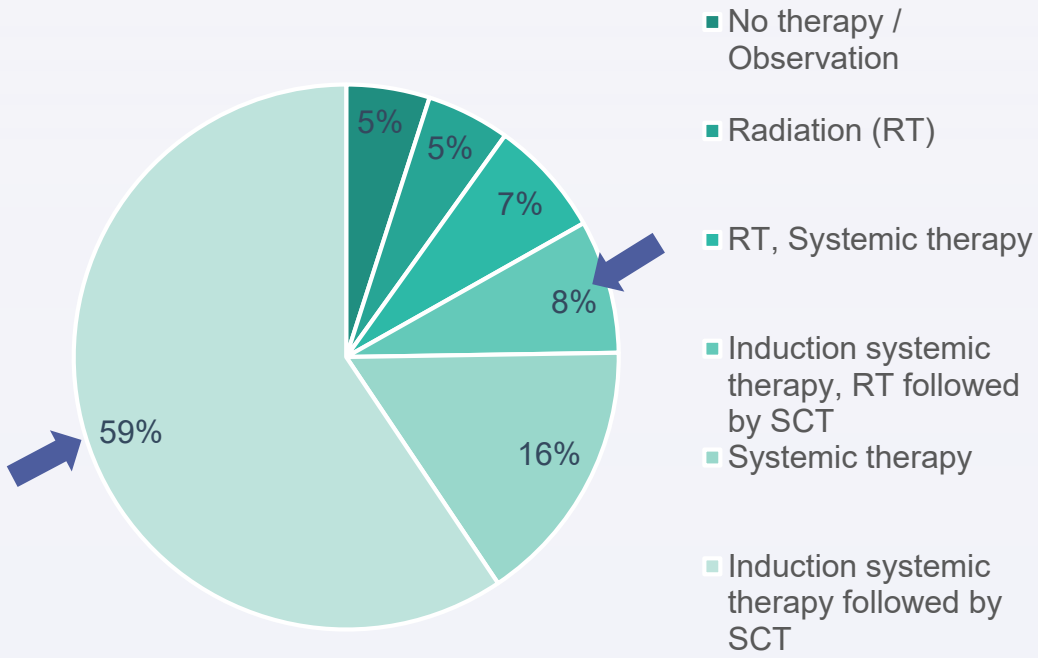
Note: "Other" category includes various therapies used in <5% of patients each.
*QM8 (transplant-eligible n=72, transplant-ineligible n=72): What percent of newly-diagnosed multiple myeloma patients are treated with each of the modalities listed below?

~62% (US) and ~68% (EU) of NDMM patients eligible for SCT will receive it

Initial Treatment Modality Utilization for Transplant Eligible Patients, Multiple Myeloma, U.S., 2020*



Initial Treatment Modality Utilization for Transplant Eligible Patients, Multiple Myeloma, EU5, 2020*

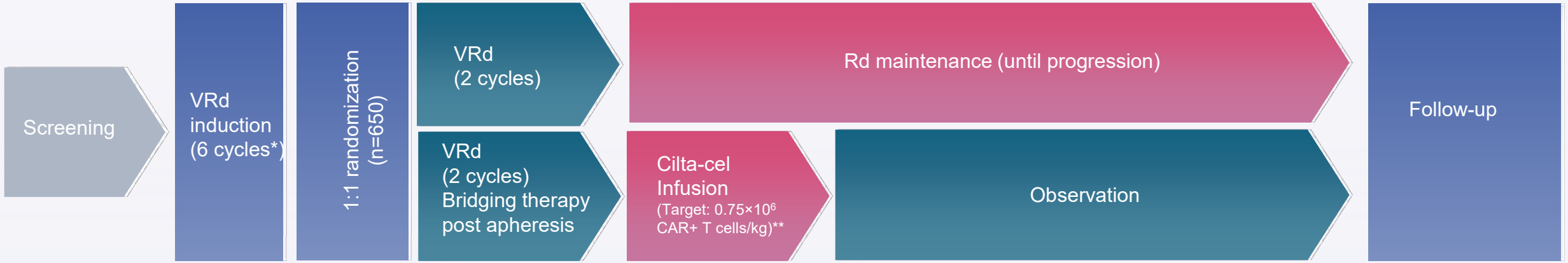


Source: CancerMPact Treatment Architecture, US and EU5, Multiple Myeloma; by Kantar, published 11/20

Note: "Other" category includes various therapies used in <5% of patients each.
*QM8 (transplant-eligible n=72, transplant-ineligible n=72): What percent of newly-diagnosed multiple myeloma patients are treated with each of the modalities listed below?

CARTITUDE-5: Phase 3 Study in newly diagnosed MM

Not intended for transplant (NCT04923893)



KEY INCLUSION CRITERIA

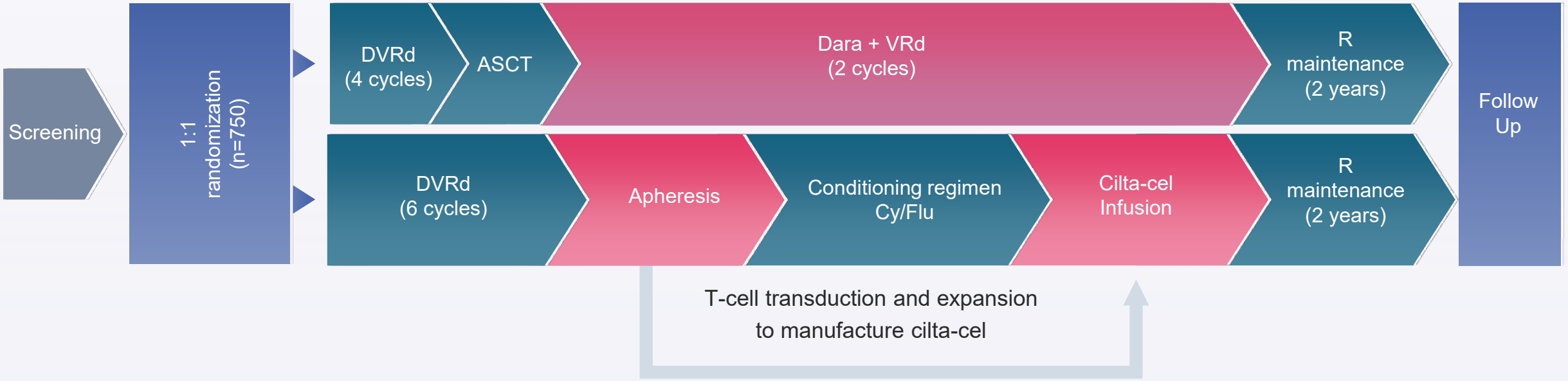
- Newly diagnosed multiple myeloma
- Not considered candidate for high-dose chemotherapy with ASCT due to advanced age or presence of comorbid condition(s) or defer high-dose chemotherapy with ASCT as initial treatment
- Frailty index of ≥2 according to Myeloma Geriatric Assessment
- Prior CAR-T or BCMA-targeting therapy
- Any prior therapy for multiple myeloma or smoldering myeloma

STATUS

- Study start date: August 2021
- ~118 study locations

VRd: Darzalex, Revlimid, dexamethasone; Rd: Revlimid, dexamethasone; ASCT: autologous stem cell transplant; * Participants who received 1 cycle of VRd therapy prior screening, will only receive 5 cycles of VRd.
** Conditioning regimen: cyclophosphamide/ fludarabine; Study start/locations source: clinicatrials.gov

CARTITUDE-6: Phase III Study in newly diagnosed MM who are transplant eligible (NCT05257083)



KEY INCLUSION CRITERIA

- Newly diagnosed multiple myeloma
- Intended for ASCT
- No Prior CAR-T therapy (any target)
- No Prior BCMA directed therapy or prior therapy for MM or SMM

STATUS

- Not yet recruiting
- Collaborative study with European Myeloma Network(EMN)
- Conducted worldwide

ASCT: autologous stem-cell transplant; CAR-T, chimeric antigen receptor-T cell; DVRd, daratumumab, bortezomib, lenalidomide, dexamthesone; R: Revlimid; MM, multiple myeloma; SMM: smoldering multiple myeloma. Study start/locations source: clinicatrials.gov

Current Use of ASCT and Potential Role of CART in NDMM

100 NDMM patients

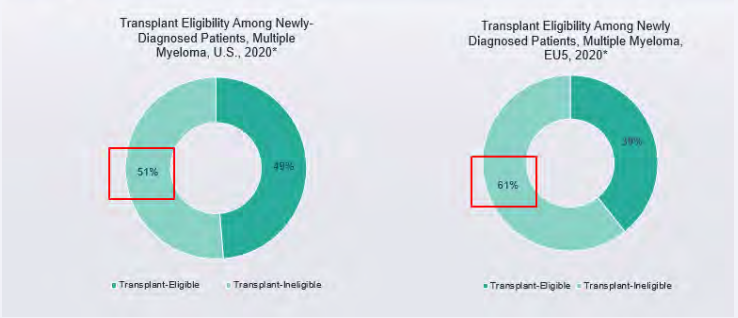
~50- 60% Transplant ineligible

~15% will be eligible BUT DEFERRING transplant

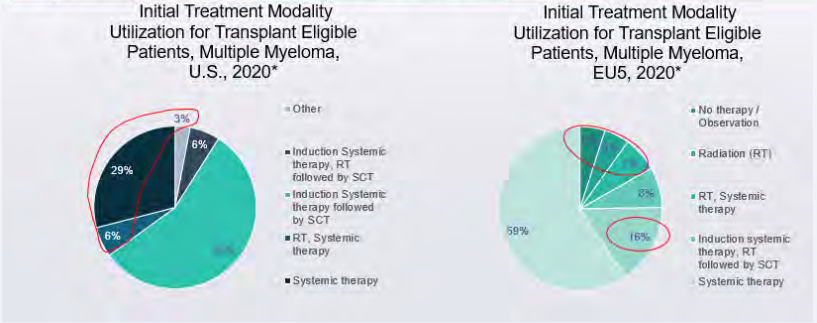
~25% will be eligible and RECEIVE transplant

- ~13-59% will have optimal response*
- ~ 30-40 % will have sub-optimal response*
- ~ 5-20 % will have no response*

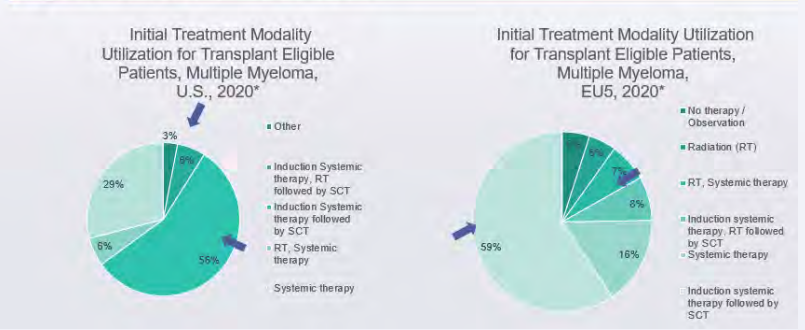
~51% (US) and ~61% (EU) of NDMM Patients are Ineligible for Transplant



~38% (US) and ~32% (EU) of NDMM patients are eligible for SCT, but do not receive it initially



~62% (US) and ~68% (EU) of NDMM patients eligible for SCT will receive it



Targeted by CARTITUDE-5

Targeted by CARTITUDE-6

Source: CancerMPact Treatment Architecture, US and EU5, Multiple Myeloma; by Kantar, published 11/20

* Dhakal at al., *JAMA* 2018; Attal at al. *NEJM* 2017; Vij at al., *Biology of Blood and Marrow Transplantation* 2015

CARTITUDE-5

Frontline: Transplant not intended (TNI)*

Phase 3 Global BCMA CAR-T Cell Therapy Clinical Trial in Frontline Setting

Commercial Assumptions/Implications

- CARVKTI™ potential indication assumption
  - 64,000 newly diagnosed patients across US/EU/Japan
  - *Transplant not intended eligible patient populations
    - 50% US: ~17,000
    - 40% EU: ~9,500
    - 45% Japan: ~3,000
  - If approved, indication may represent a significant downstream cost avoidance opportunity

Opportunity Assessment

** Transplant not intended (TNI) = clinically transplant ineligible + clinically transplant eligible but deferred*
Source: Kantar Health, Precision-IQ, SHS/Komodo Claims

CARTITUDE-6

Frontline: Transplant Eligible

First Global Phase 3 clinical study comparing a BCMA CAR-T therapy to ASCT in newly diagnosed multiple myeloma

Commercial Assumptions/Implications

- Potential for early, durable responses in a frontline setting may provide significant downstream cost avoidance opportunities

- CARVYKTI potential indication assumption
  - ~64,000 newly diagnosed patients across US/EU/Japan
  - Transplant Eligible Populations
    - US: ~10,000
    - EU: ~8,500
    - Japan: ~1,000

Competitive Assumption

- No current Ph3 registrational studies on CT.gov for this patient population investigating a BCMA CAR-T versus ASCT

Opportunity Assessment

Source: Kantar Health, Precision-IQ, SHS/Komodo Claims

Coffee Break

The presentation will resume in 15 minutes

LEGEND BIOTECH

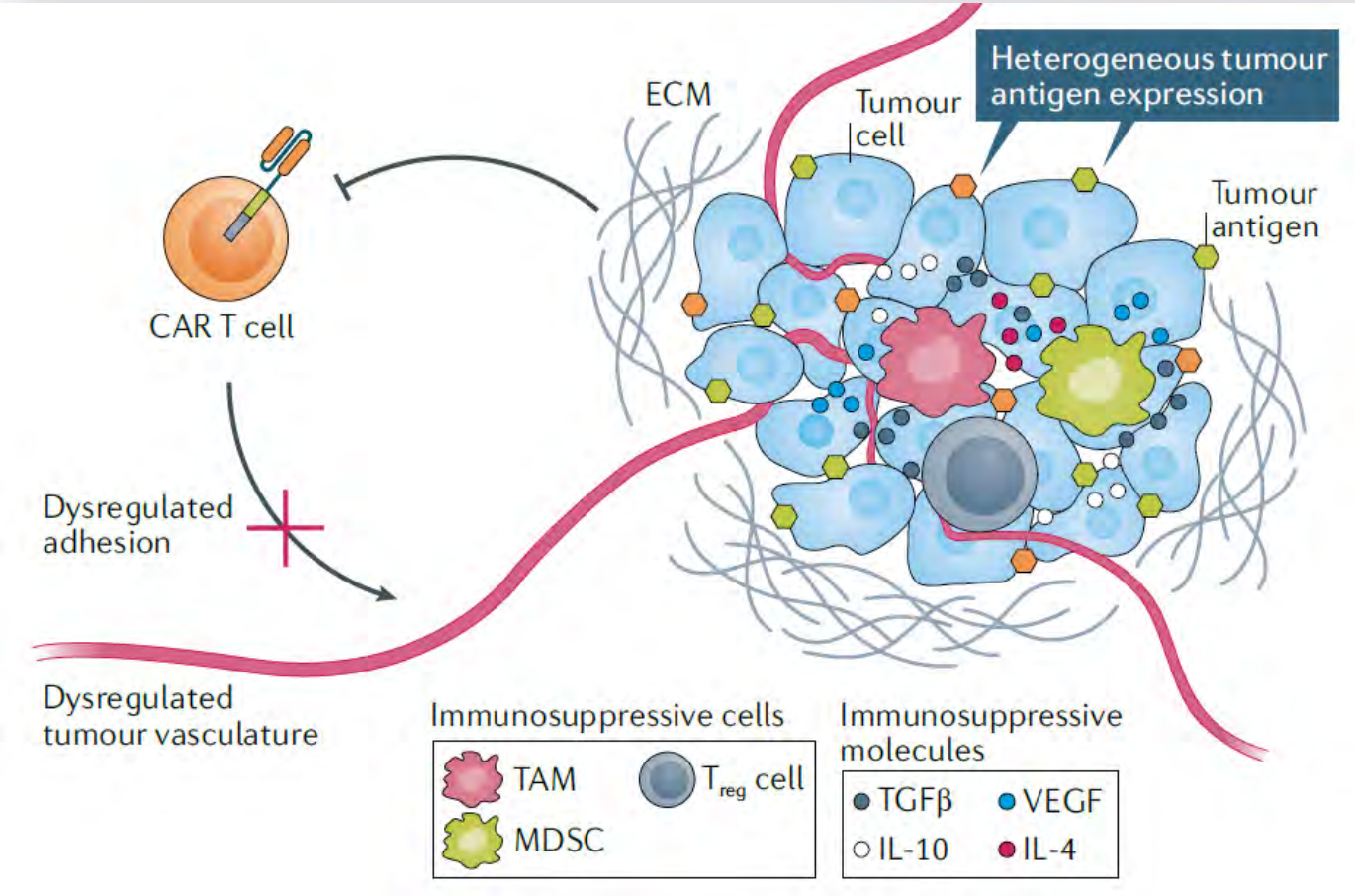
In Fierce Pursuit of Novel Therapies

Guowei Fang, Ph.D.
Senior Vice President, Research and Early Development

R&D Outline

Next Frontier in Cell Therapy: how to realize its full potential

Despite tremendous progress, challenge & opportunity remain



(Andrew J. Hou et al 2021)

On Tumors

- Antigen heterogeneity & downregulation
- Immunosuppressive TME & circulating factors
- Tumor load and disease organs

On Adoptive Cell Therapy

- Insufficient expansion & persistence
- Trafficking & infiltration
- Treatment related toxicity
  - On-target/off-tumor
  - CRS, ICANS, ITP/MAS/HLH
- GvHD, HvG for allogeneic cell therapy
- Complex manufacture with high cost

Our R&D Strategy

- Invest in research to understand diseases and immune biology, to develop armors tailored to immune/tumor mechanisms, and to address GvHD & HvG
- Establish differentiated proprietary allogeneic platforms in CAR αβT, NK and γδ T
- Develop allogeneic products for blood cancers (MM, AML, and/or NHL)
- Develop autologous and/or allogeneic products specifically addressing TMEs in solid tumors
- Support IIT studies to accelerate clinical POC for new platforms and products

DISEASE AREAS
Hematologic malignancies
Solid tumors

CORE TECHNOLOGIES
CAR-T
NK
γδ - T

PRODUCT PLATFORMS
Autologous
Allogeneic

Our Approaches

Abs Screening & Engineering
- High-throughput sdAbs screening
- High specificity & affinity
- Multi-specific CAR platform

Innovative CAR Enhancing Strategies
- Leverage learnings from cilta-cel
- Innovative CAR modalities
- Enhanced immune synapse

Patient-Driven Clinical Strategy
- Differentiated clinical strategy
- Robust translational medicine support
- Fast route to clinical POC via IIT studies

Complementary Suite of Technologies

Unique binders	TME-driven armor strategy	Optimized CAR	Smart manufacture process	Clinical strategy

- *Enhanced immune cell expansion and persistence*
- *Improve immune cell trafficking and infiltration*
- *Overcome TME suppression*

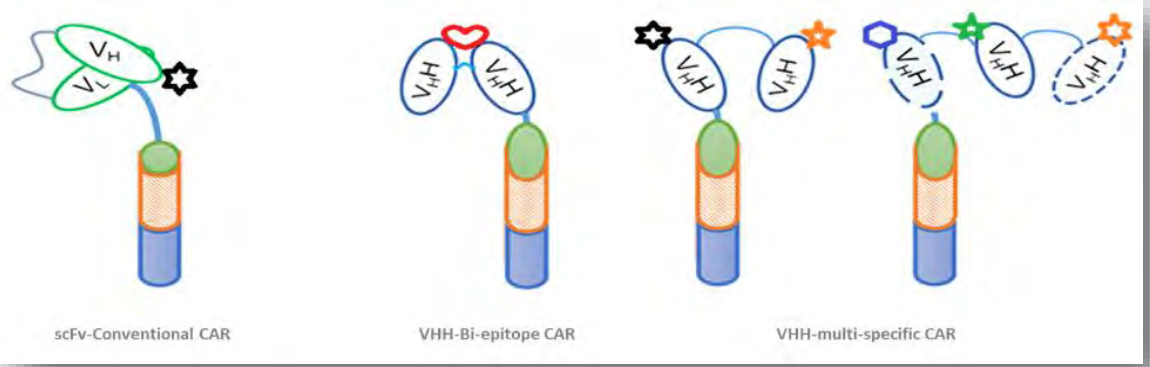
Diverse Armor MOAs under Development
- Cytokines
  - Membrane anchored, mutations, intracellular trapped
- TME specific armors
  - TME factor trappers, switch receptors
- Innate immune armors
- Intracellular modulators

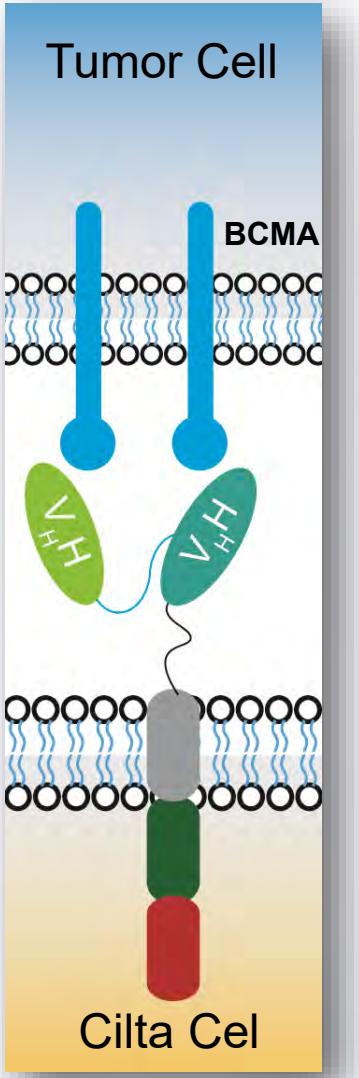
Diverse Allogeneic Platforms
- Non-gene editing universal CAR-T to address GvHD
- Diverse approach to manage HvG
- Differentiated and proprietary CAR αβT, NK and γδ T

Legend VHH-Based **Multi-Specific CAR Platform**

When compared to fragment antigen-binding antibodies:

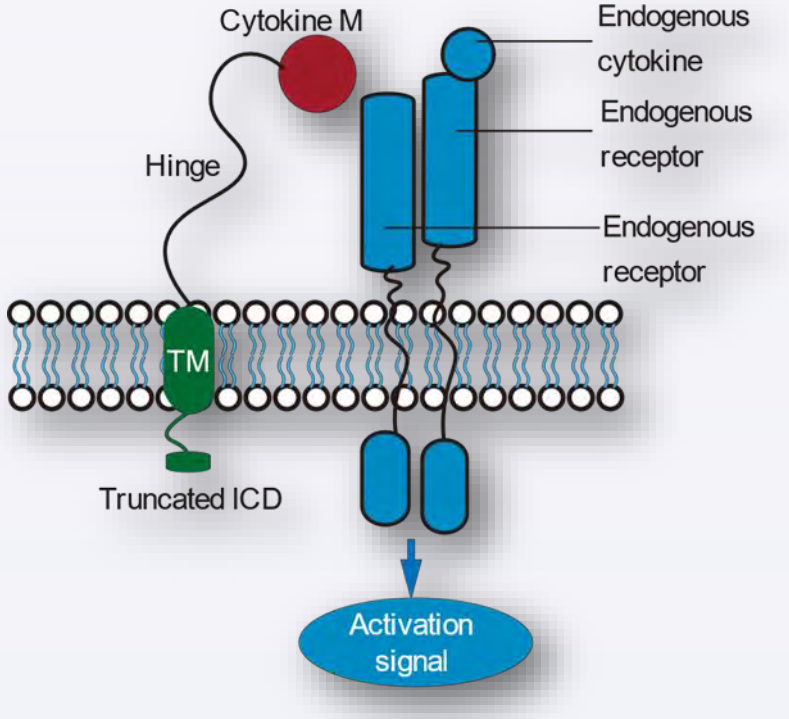
- Improved CAR expression and stability
- Access to novel and hidden epitopes with membrane proximal binders
- Robust engineering flexibility for the design of complex multi-specific CAR
- Enhanced immune synapse formation and better immune cell activation



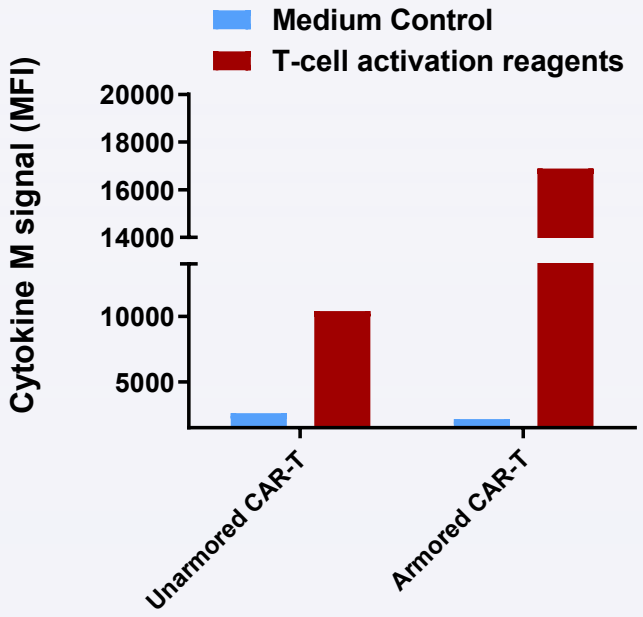


Armor: Membrane Anchored Cytokine Enhances Immune Cell Expansion

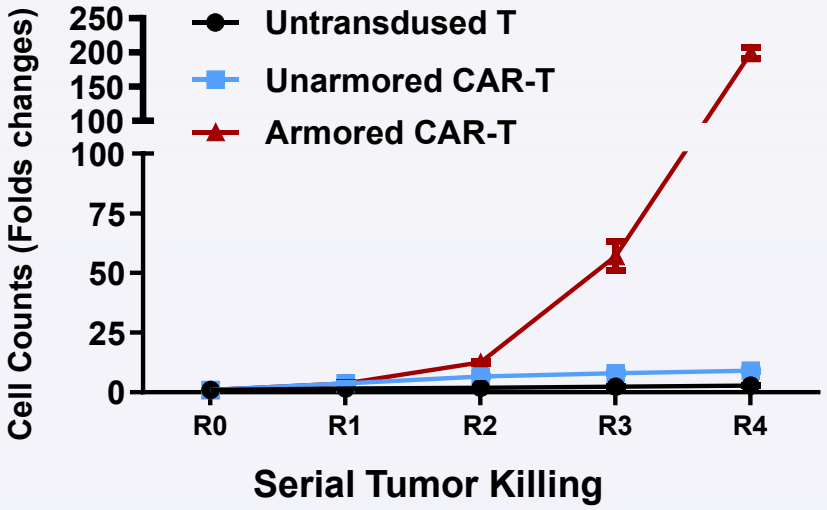
Armor Design



Active cytokine M signaling



Improved target-dependent CAR-T expansion under repetitive tumor challenges

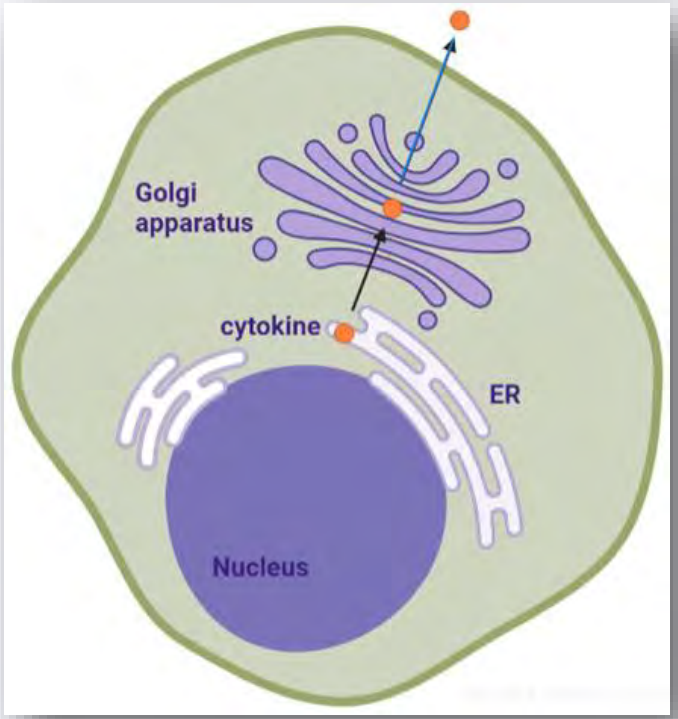


- Engineer membrane bound cytokine designed to improve safety
- Promote immune cell expansion and persistence

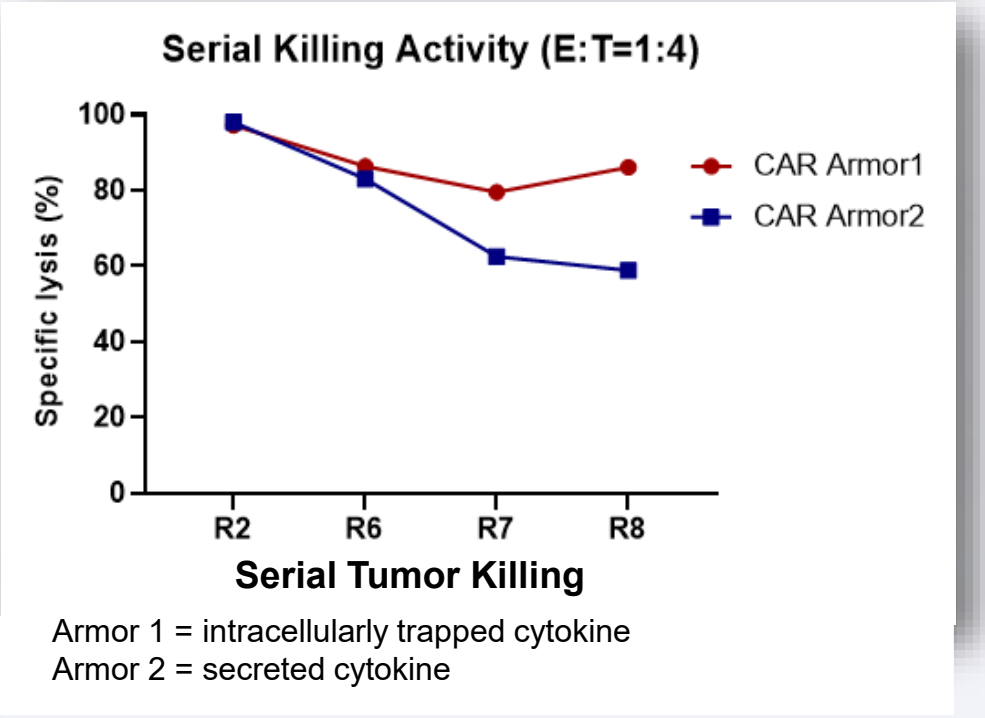
Armor: Intracellular Cytokine Trapper Enhances Immune Potency & Safety

Armor Design

Block secretion of cytokine

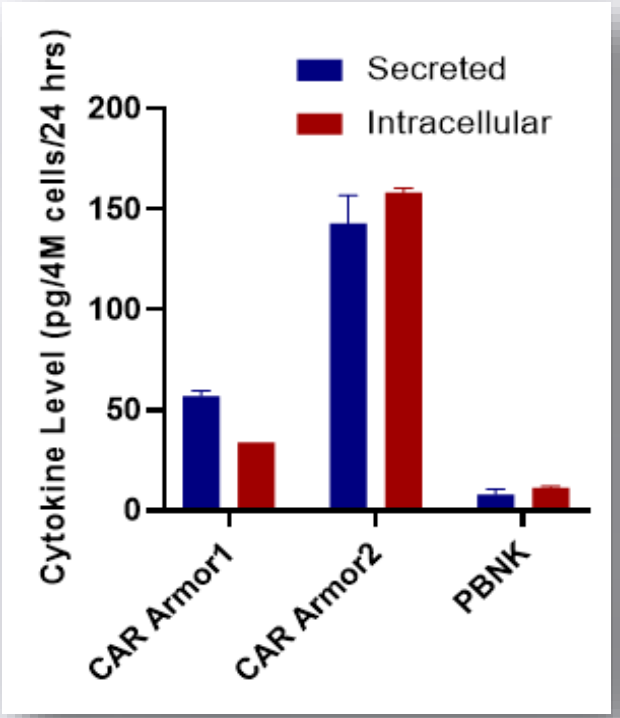


Repetitive Tumor Killing in vitro



Armor 1 = intracellularly trapped cytokine
Armor 2 = secreted cytokine

Cytokine Level

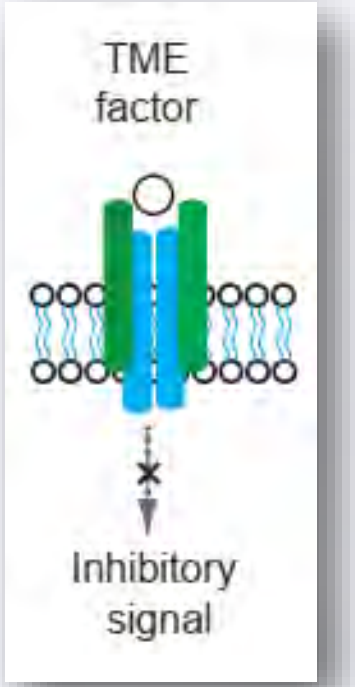


- Enhance immune cell potency, expansion & persistence
- Designed to improve safety

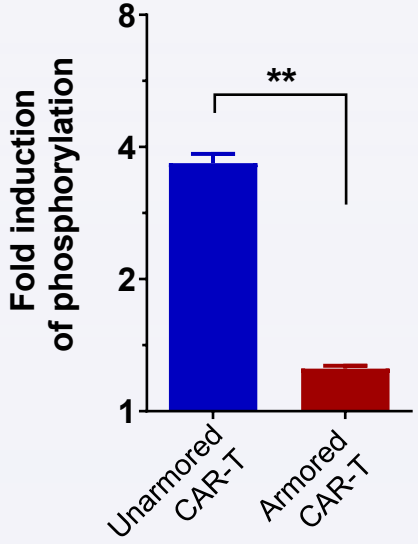
This presentation is for investor relations purposes only – Not for product promotional purposes

Armor: TME Factor Trapper Overcomes Hostile Tumor Microenvironment

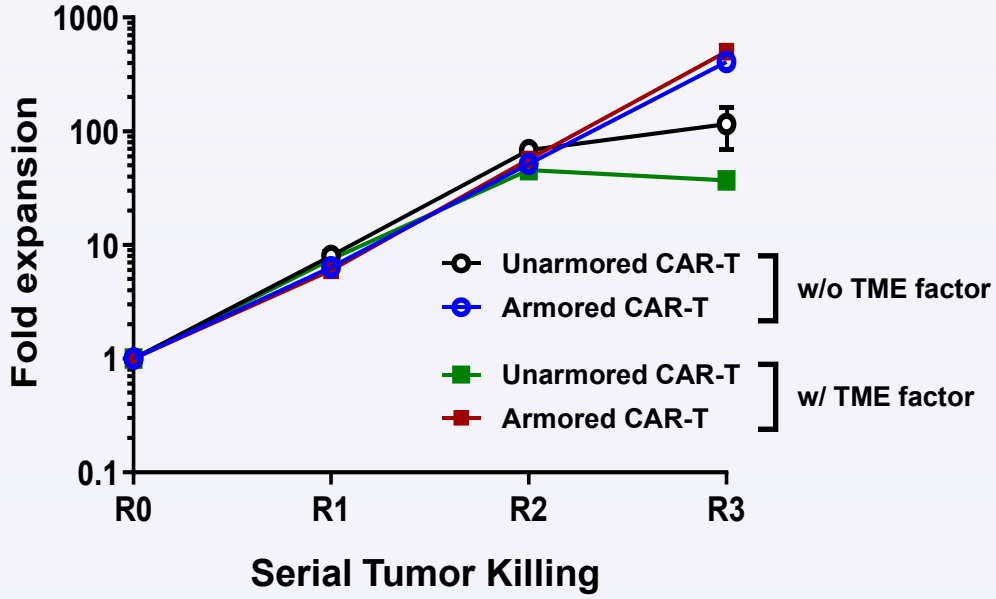
Armor Design



Blocking TME-mediated inhibitory signaling



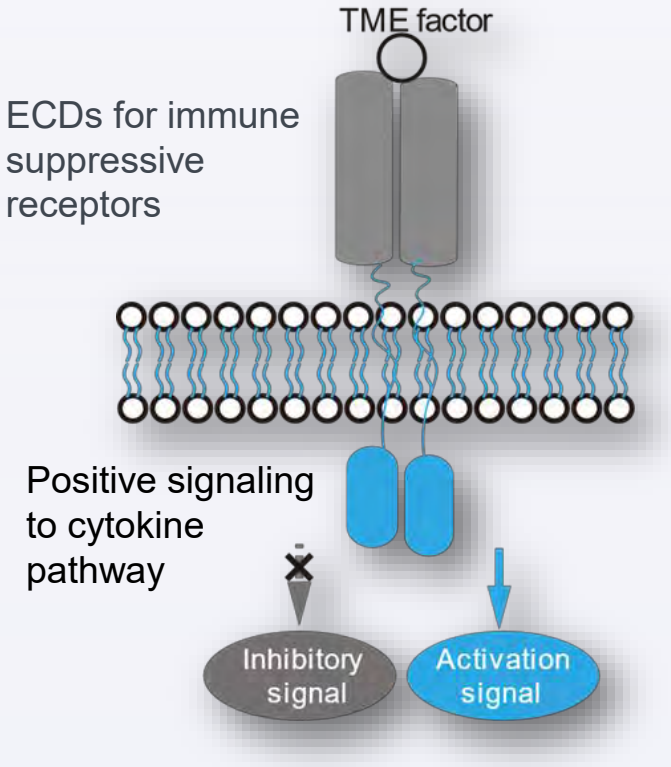
Preserving proliferative capacity in the presence of immune suppression



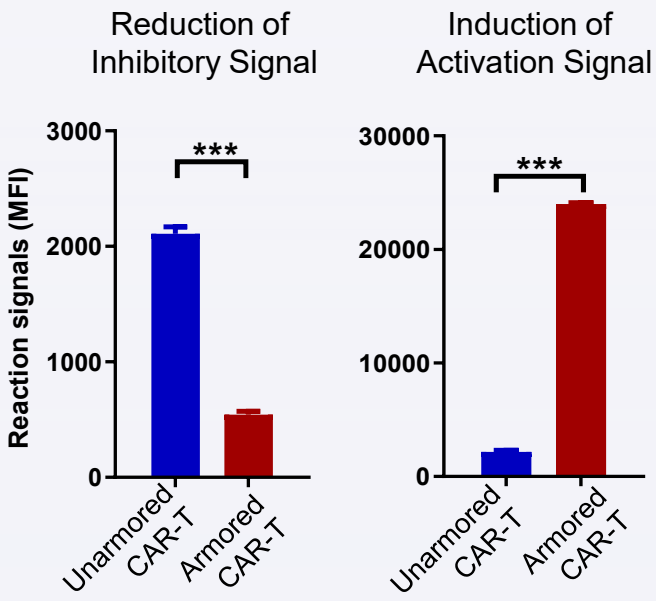
- Block immune-suppressive signaling derived from hostile TME
- Preserve metabolic fitness and prevent T cell exhaustion
- Enhance immune cell infiltration into TME

Armor: Switch Receptor Converts Immunosuppression to Immune activation

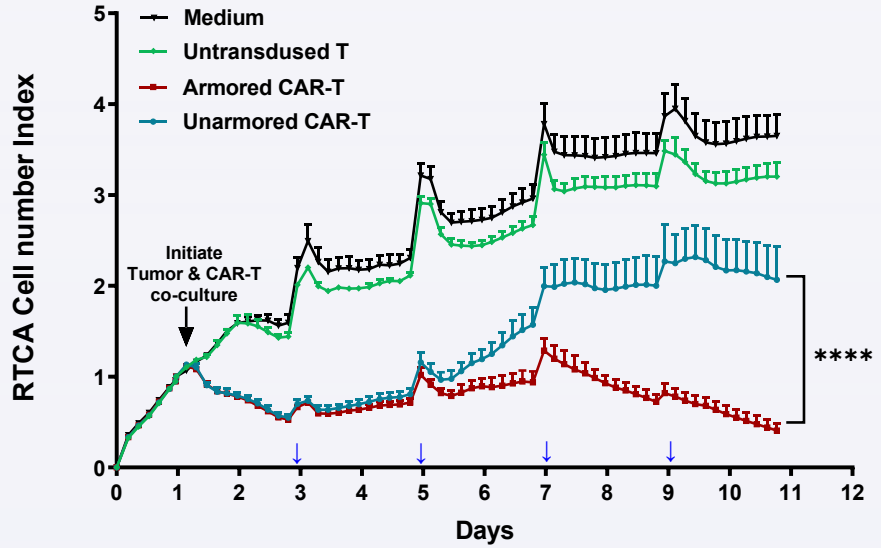
Armor Design



Signal Conversion with TME Factor



Enhanced Long-Term Cytotoxicity Potency *



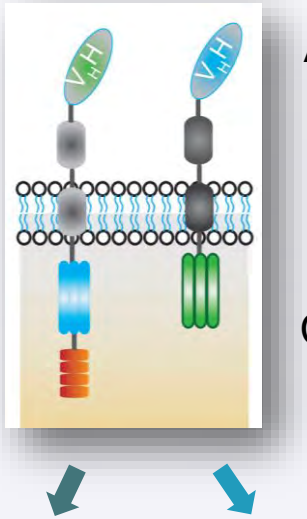
* Long-term Co-culture Assay Monitored by RTCA, with CAR-T : Hep3B2.1-7 ratio at 1:50.
↓Co-culture medium were refreshed every 2 days to allow healthy grow of CAR-T and tumor cells

- Utilize TME suppressive factor for immune activation
- Confer resistance to TME mediated immune inhibition and exhaustion
- Enhance immune cell expansion and persistence

Armor: Innate Armor Drives Immune Cell Expansion and Potency

Armor Design

Antigen binding domain 1



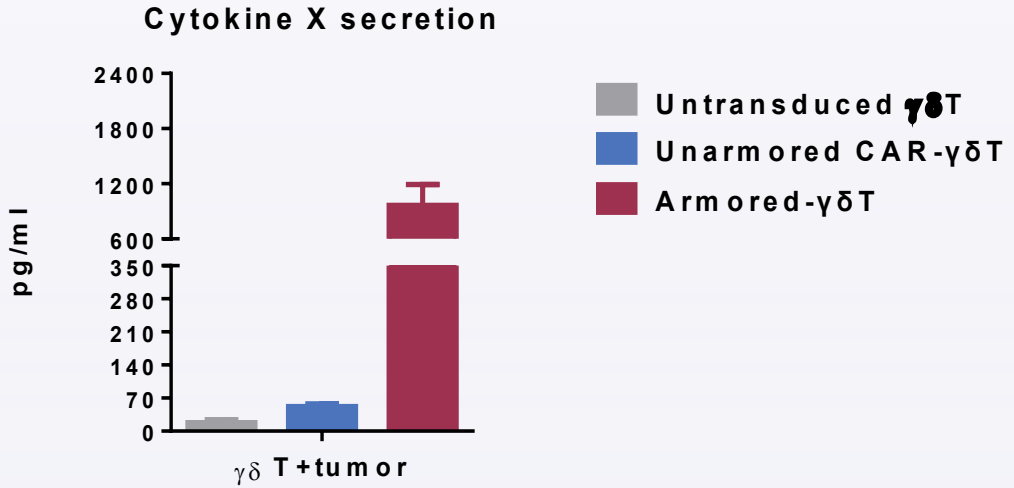
Antigen binding domain 2

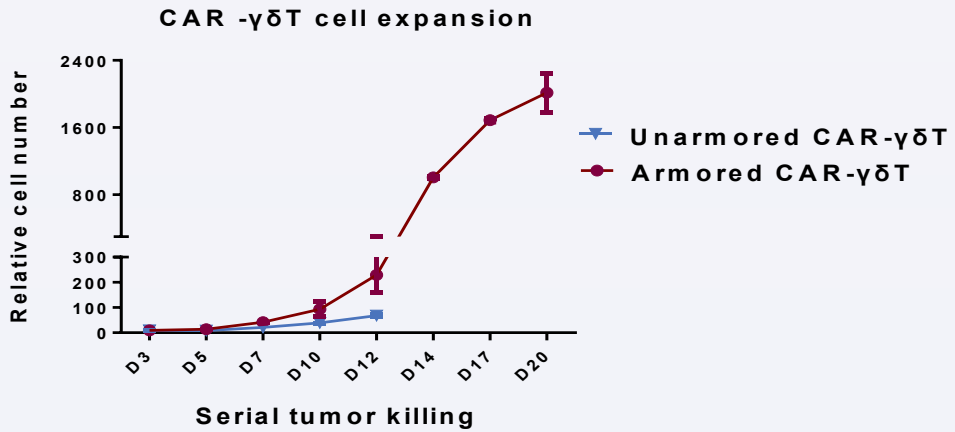
Signaling from adaptive immunity

Co-signaling from innate immunity

Activation and cytotoxicity

Cytokine X secretion and immune cell expansion

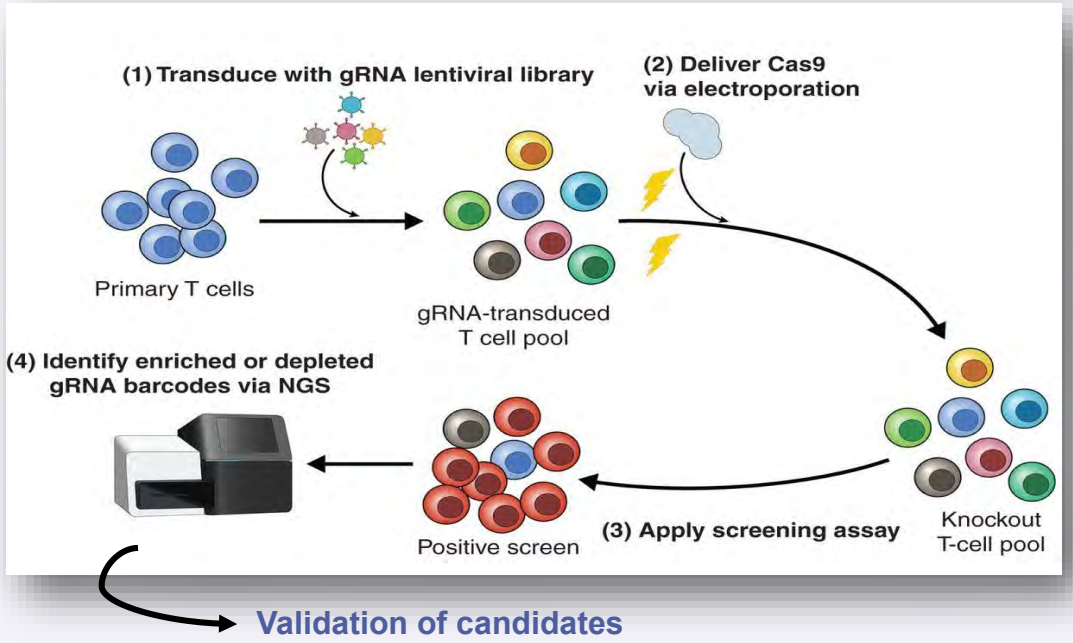




- Potent & selective cytotoxicity
- Robust cell expansion/persistence

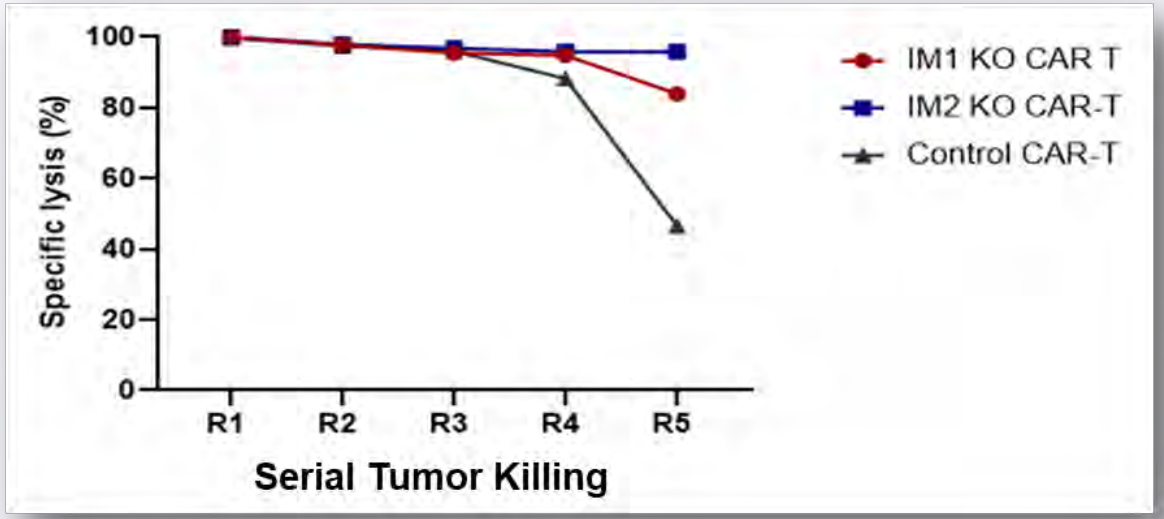
Armors: Intracellular Modulators (IM)
Identified by Functional Genomic Screen

Experimental Design

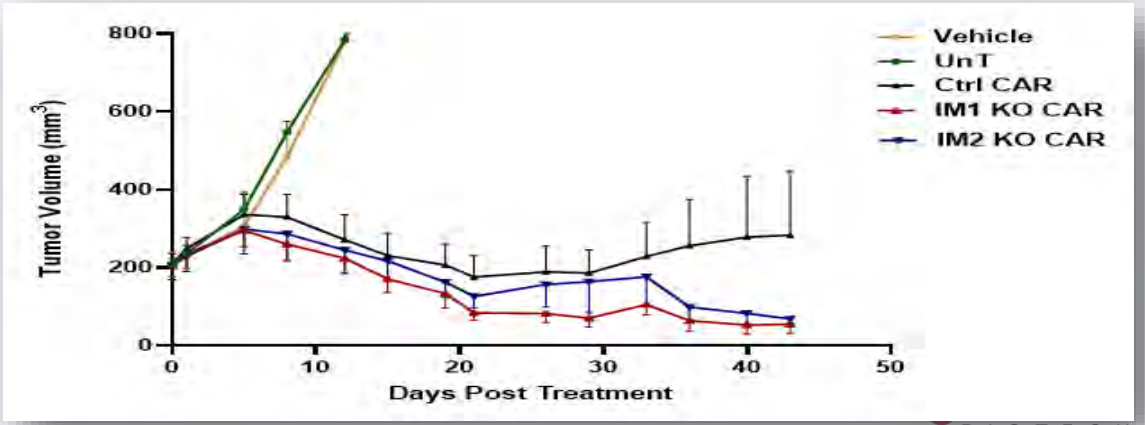


- Improve immune cell fitness and persistence in tumor microenvironment
- Novel and differentiated MOAs

Serial Killing of Tumor Cells



Anti-Tumor Efficacy in vivo

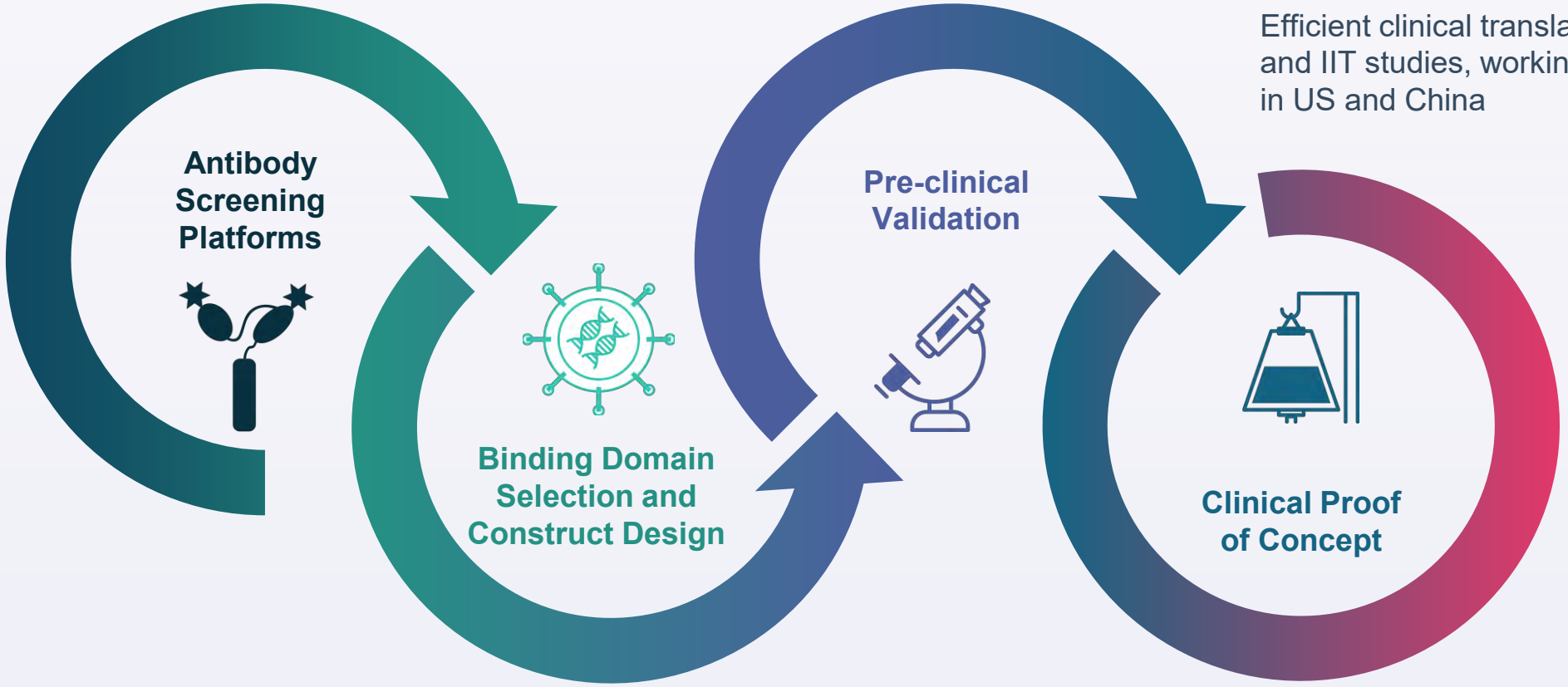


Our End-to-End R&D Capability

High-throughput antibody screening and engineering capability, including single-domain antibodies generated from llama and conventional antibodies

Robust *in vitro* and *in vivo* screening platforms to prioritize pipeline assets

Efficient clinical translation with IND and IIT studies, working with KOLs in US and China



Proprietary methodology to optimize the selection of binding domains and design CAR-T constructs with two or more antigen-binding domains

CMC Manufacturing

Our Pipeline

Global | US | China

Preclinical

NSCLC
(GPC3)
Autologous

GASTRIC & ESOPHAGEAL
(CLAUDIN 18.2)
Autologous

COLORECTAL
(GCC)
Autologous

SCLC
(DLL3)
Autologous

Phase 1

NHL† /ALL†
(CD19 X CD20 X CD22)†
Autologous
NCT05318963
NCT05292898

RRMM (BCMA)
LEGEND-2†
Autologous
NCT03090659

GASTRIC, ESOPHAGEAL & PANCREATIC†
(CLAUDIN 18.2)
Autologous
NCT04467853

HCC†
(GPC3)
Autologous
NCT05352542

RRMM†
(BCMA)‡
Allogeneic
NCT05376345
NCT05498545

Phase 2

RRMM (BCMA)*
CARTIFAN-1
Autologous
NCT03758417

RRMM (BCMA)*
CARTITUDE-1
Autologous
NCT03548207

MM (BCMA)*
CARTITUDE-2
Autologous
NCT04133636

Phase 3

RRMM (BCMA)*
1-3 Prior Lines
CARTITUDE-4
Autologous
NCT04181827

NDMM (BCMA)*
Transplant Not Intended
CARTITUDE-5
Autologous
NCT04923893

NDMM (BCMA)*
Transplant Eligible
CARTITUDE-6
Autologous
NCT05257083

*In collaboration with Janssen, Pharmaceutical Companies of Johnson & Johnson.
†Phase 1 IIT in China.
‡Multiple allogeneic platforms are being developed.

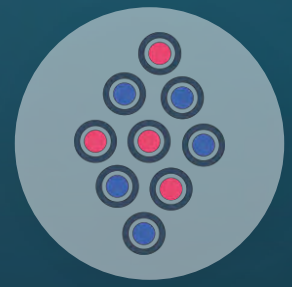
ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; BCMA, B-cell maturation antigen; DLL3, delta-like ligand 3; GPC3, glypican-3; GCC, guanylyl cyclase C; HCC, hepatocellular carcinoma; IIT, investigator-initiated trial; MM, multiple myeloma; ND, newly diagnosed; NHL, non-Hodgkin lymphoma; NSCLC, non small cell lung cancer; RRMM, relapsed or refractory multiple myeloma; SCLC, small cell lung cancer.

LEGEND BIOTECH

Solid Tumors

LB1908, LB2101, & LB2102

Solid Tumors



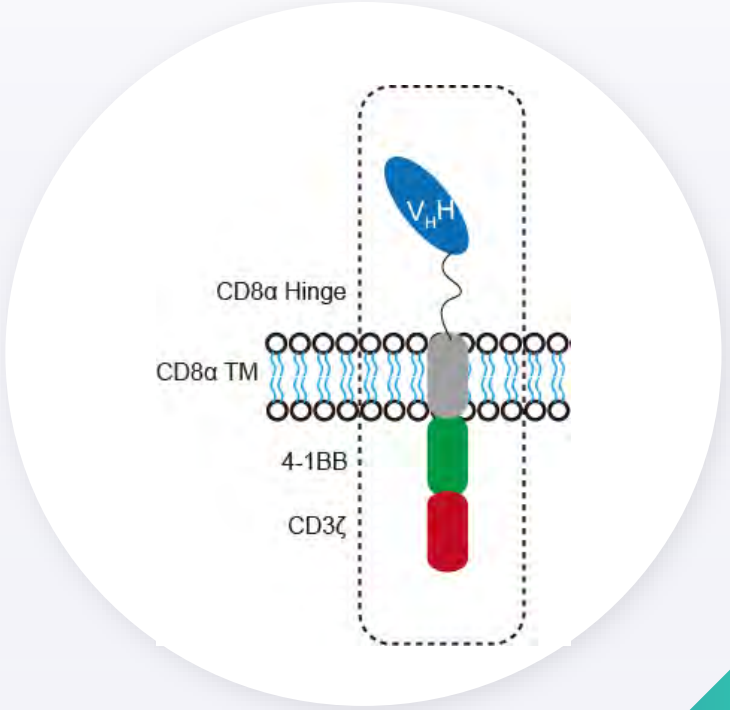
Allogeneic Platforms

LB1908 (LCAR-C18S): Legend CAR-T Targeting CLDN18.2

For gastric cancer, esophageal cancer and pancreatic cancer

TARGET

- Claudins (CLDN) are a family of tight junction proteins[1]
- CLDN18.2 is expressed in gastric cancer and pancreatic cancer[2]
- CLDN18.2 is highly conservative cross species



MOA/SCIENTIFIC RATIONALE

- LB1908 targets CLDN 18.2 via a proprietary VHH antibody
- High selectivity against the closely related CLDN 18.1

CLINICAL DEVELOPMENT STRATEGY

- First-In-Human IIT study is ongoing for clinical POC
  - Adult Claudin 18.2 positive patients with recurrent or metastatic advanced solid tumors (including advanced gastric cancers and non-gastric cancers) and have failed prior lines of systemic treatment
  - Enrollment in the China IIT is ongoing to evaluate safety and tolerability
- US IND was cleared on June 1, 2022

[1] Zhang J, et al. Chin J Cancer Res. 2020 Apr;32(2):263-70.
[2] Sahin U,et al. Clin Cancer Res. 2008 Dec 1;14(23):7624-34

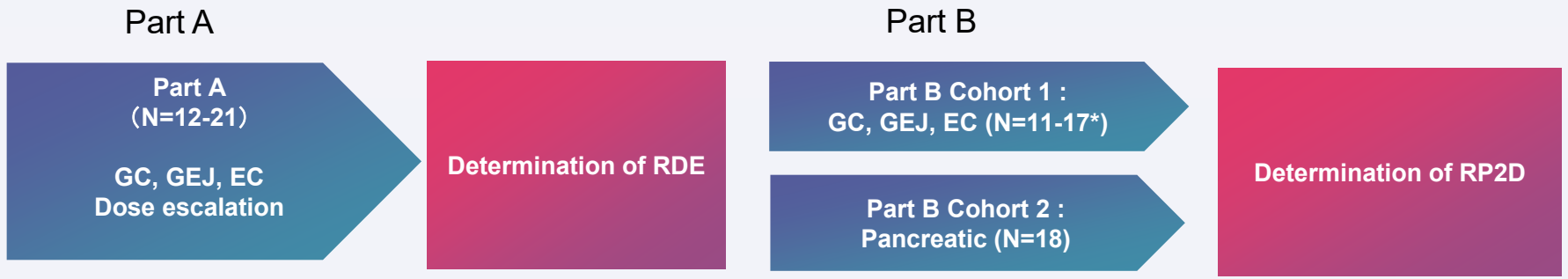
LB1908: US IND study in Claudin18.2-positive advanced solid tumors

TARGET POPULATIONS

- Histologically/cytologically confirmed unresectable, locally advanced or metastatic adenocarcinoma of the stomach, GEJ, or distal esophagus; adenocarcinoma of the pancreas will be included in part B
- Having failed at least one line of prior standard therapy
- Immunohistochemistry of tumor tissue samples indicates Claudin18.2 positive

TRIAL FLOW

STUDY DESIGN



* subjects will be pooled to make 23 subjects treated at RDE

RDE (recommended dose for exposition), RP2D (recommended phase 2 dose), GC(gastric cancer), GEJ(gastro esophageal junction cancer), EC (esophageal cancer)

LB2101 (LCAR-H93T): Legend Armored CAR-T Targeting GPC3

For HCC and NSCLC

TARGET

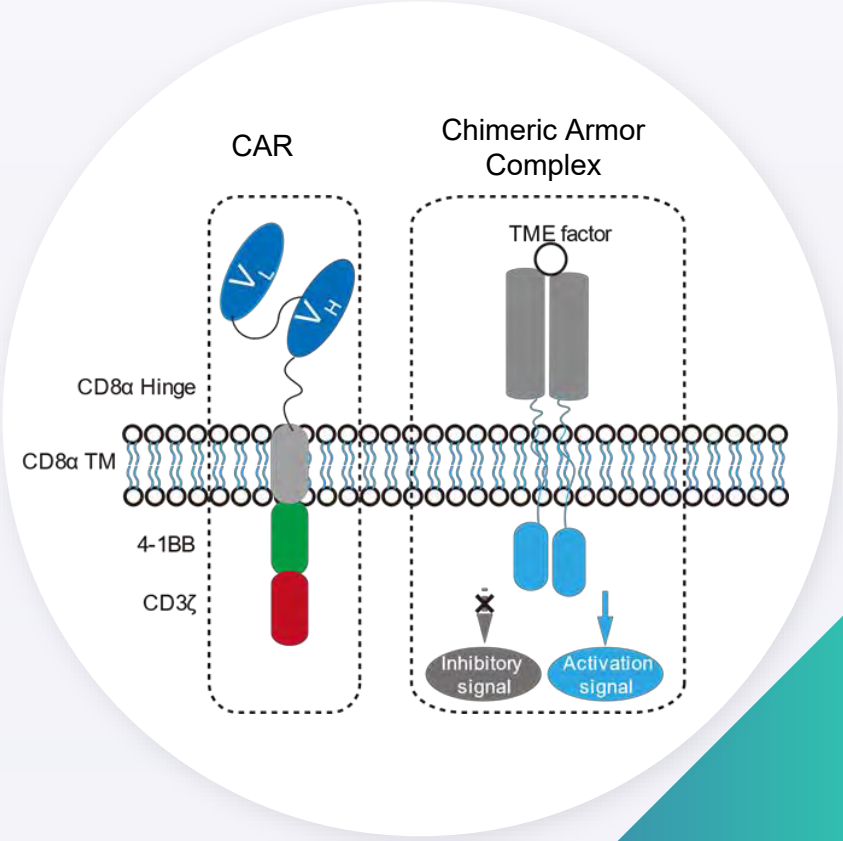
- GPC3 is a promising target specifically over-expressed in solid tumors
- Significantly upregulated in HCC (76%), lung SCC (52%), esophageal SCC (27%), germ-cell tumors (44-100%), ovarian clear cell cancer (41%) and serous cancer (11%) et al.[1]

MOA/SCIENTIFIC RATIONALE

- In house developed humanized scFv with high affinity and specificity to GPC3
- Innovative armor platform: Utilize immunosuppressive signal in TME to augment CAR-T potency
- Optimized CAR design outperformed benchmarks *in vivo*

CLINICAL DEVELOPMENT STRATEGY

- First-In-Human study in China ongoing for clinical POC
  - Adult patients with advanced HCC; Progression or intolerance after previous standard systemic therapy
  - Immunohistochemistry of tumor tissue samples indicates GPC3 positive
  - First patient was dosed in June 2022



GPC3=Glypican 3; HCC=hepatocellular carcinoma; SCC=squamous cell cancer; TME=tumor microenvironment

[1]*Am J Pathol. 2018 Sep;188(9):1973-1981*

LB2102: Legend Armored CAR-T Targeting DLL-3

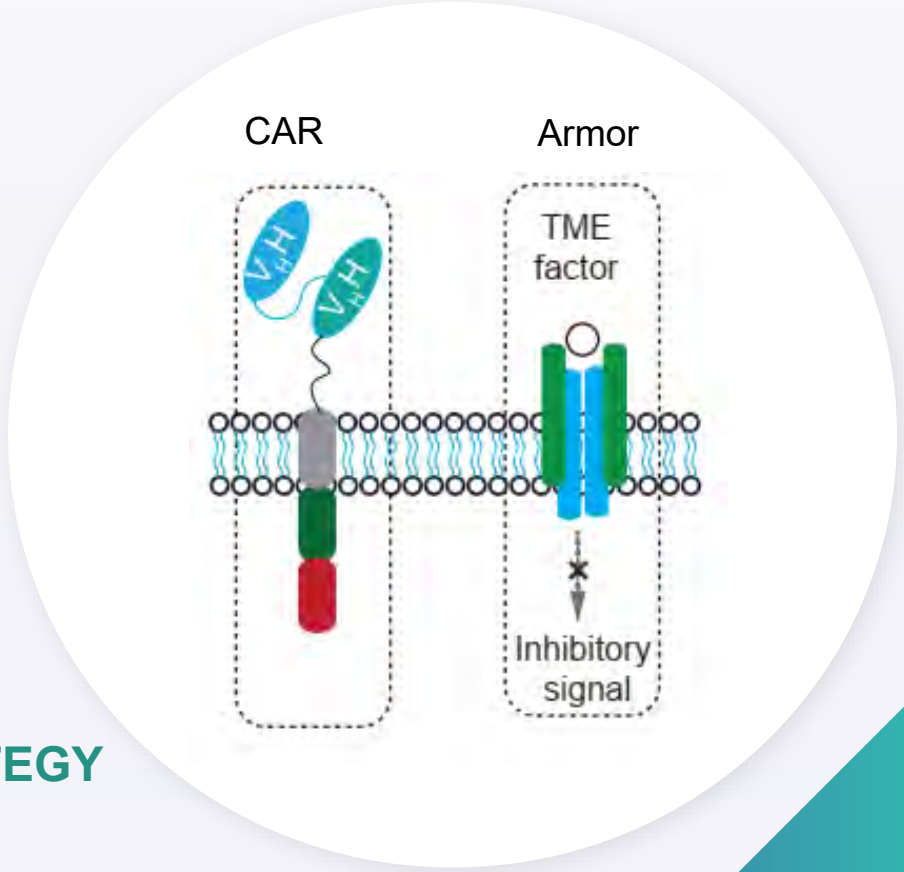
For SCLC

TARGET

- DLL-3, a promising target with prevalent & homogeneous expression in SCLC (~80% positive) and other neuroendocrine tumors
- Minimal to no expression in normal tissues
- SCLC has limited treatment options & high unmet needs

MOA/SCIENTIFIC RATIONALE

- Tandem humanized binders with high affinity and specificity
- An armor overcoming suppressive TME to promote CAR-T cell expansion, persistence and infiltration



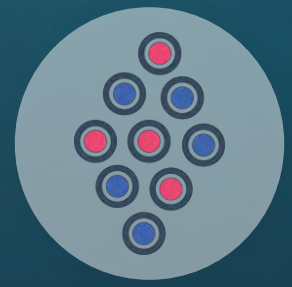
PRECLINICAL & CLINICAL DEVELOPMENT STRATEGY

- Well-tolerated *in vivo* in s.c and pulmonary orthotopic xenograft models
- US IND submission planned Q42022

Solid Tumor

LCAR-G08T

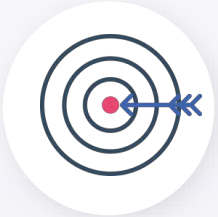
Solid Tumors



Allogeneic Platforms

LCAR-G08T: Legend Armored CAR-T Targeting GCC

For gastrointestinal cancers



TARGET

- GCC (GUCY2C) is commonly expressed in the majority of gastrointestinal malignancies, including colorectal cancer (CRC), GC, EC, GEJC, PC (large market size and high unmet medical needs)[1]
- GCC is weakly expressed in intestinal epithelial cells on the luminal membranes, avoiding systemic T cell-mediated immune responses[2]

MOA/SCIENTIFIC RATIONALE

- Humanized sdAb with high GCC binding affinity and specificity
- Potent anti-tumor efficacy in CRC animal models in comparison to benchmark
- Innovative armor platform: utilize immunosuppressive signal in TME to augment CAR-T potency

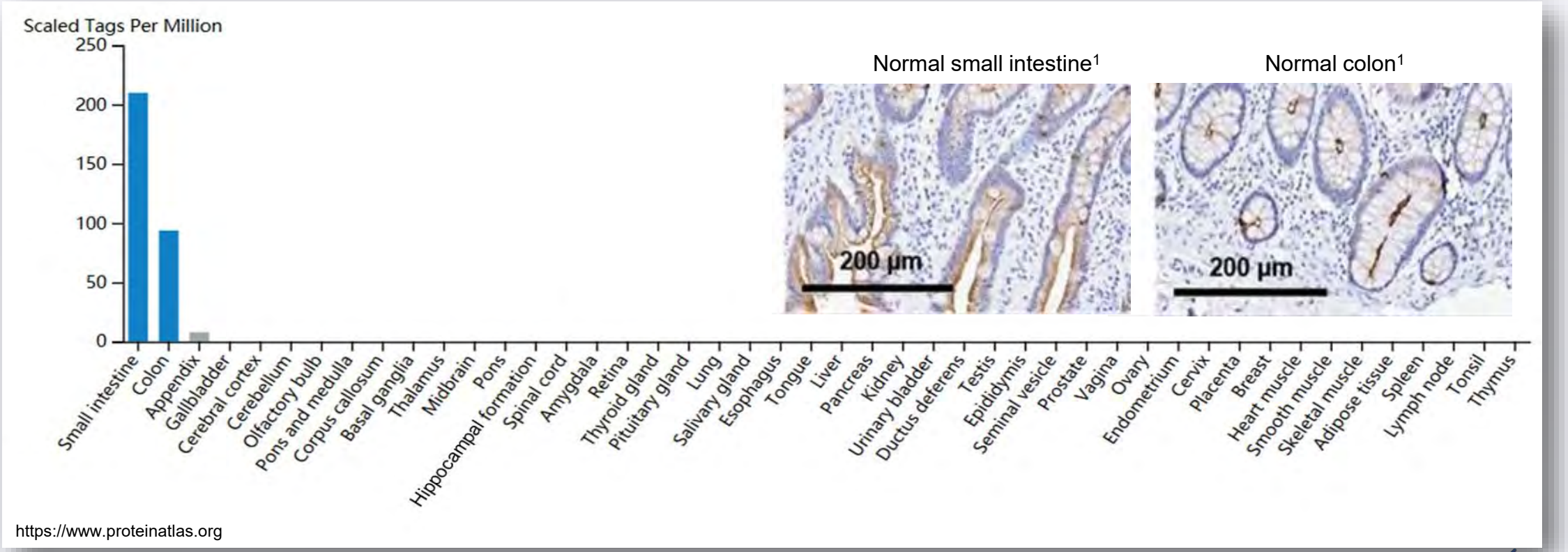
CLINICAL DEVELOPMENT STRATEGY

- First-in-human study in preparation

[1] Danaee H et al PLoS One, 2017, 12(12): e0189953.
[2] Magee M S, et al. Oncoimmunology, 2016, 5(10): e1227897.

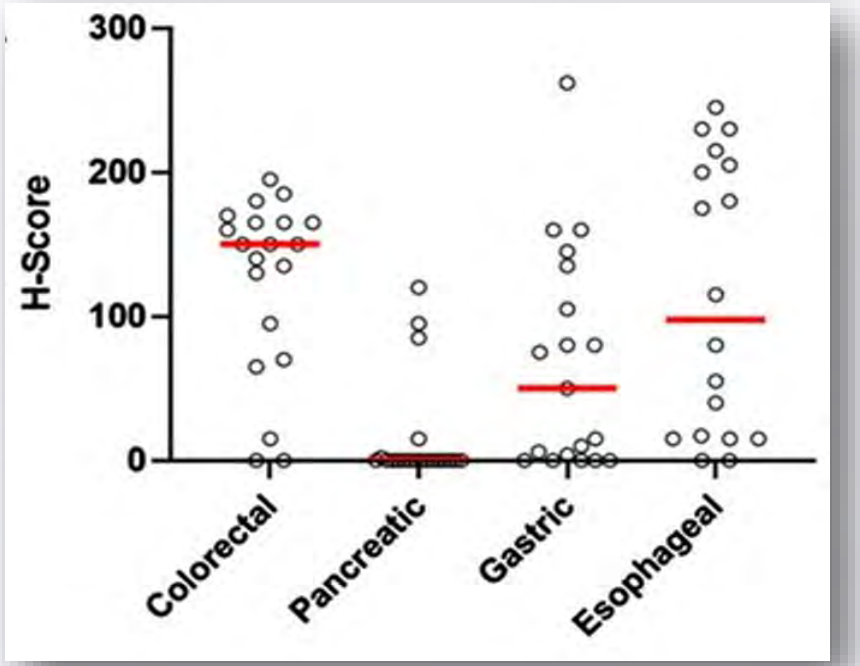
GCC is an Emerging Target for CAR-T Therapy

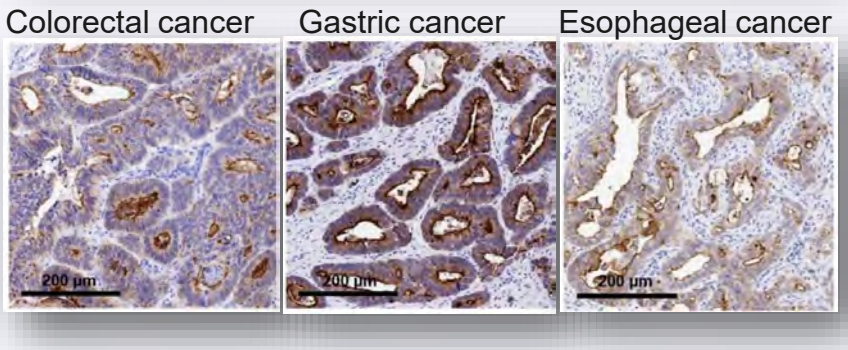
- GCC is expressed in the apical side of the epithelial brush border facing lumen, avoiding systemic T cell-mediated immune responses.[1]
- GCC CAR-T (cross-reactive with mouse GCC,MS24) accumulated in GCC+ tumors, mediating antitumor immunity, but were absent from normal intestines, which resulted in no T cell-mediated toxicity in preclinical models.[2]



[1]Mathur D et. Al. Clin Cancer Res. 2020, 26(9): 2188-2202
[2] Magee M S, et al. Oncoimmunology, 2016, 5(10): e1227897.

GCC is Widely Expressed in Gastrointestinal Cancers





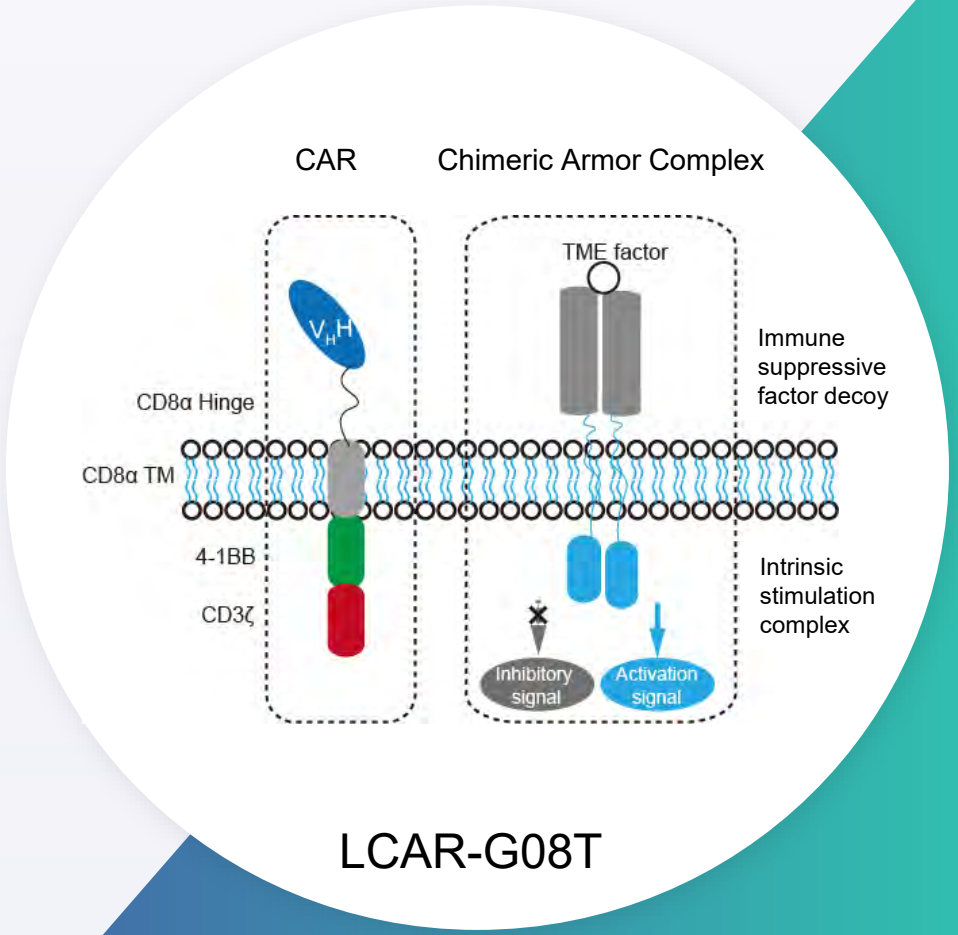
Mathur D., Root, A. et. al. Clinical Research. 2020, 26(9): 2188-2202

Indications	Global new cases per year[2~3]	GCC positive % (H-score>50)[1]
Colorectal cancer	1,800,000	85% (17/20)
Gastric cancer	1,000,000	58% (11/19)
Esophageal cancers	604,100	61% (11/18)
Pancreatic cancers	495,773	15% (3/20)

[1] Mathur D., Root, A. et. al. Clinical Research. 2020, 26(9): 2188-2202
[2] GlobalData: Colorectal Cancer-Epidemiology Forecast to 2028
[3] Cancer Statistics, 2021. CA Cancer J Clin:2021 May;7(3) 209-249.

LCAR-G08T: GCC-targeting CAR-T Cell for GI cancers

- LCAR-G08T consists of autologous T cells genetically modified to express a CAR utilizing a lentiviral vector
- Humanized sdAb with high GCC binding affinity and specificity
- Humanized sdAb-derived CAR-T with greater efficacy in animal models to benchmark
- Legend's innovative armor converts immunosuppressive signal in TME to augment CAR-T potency



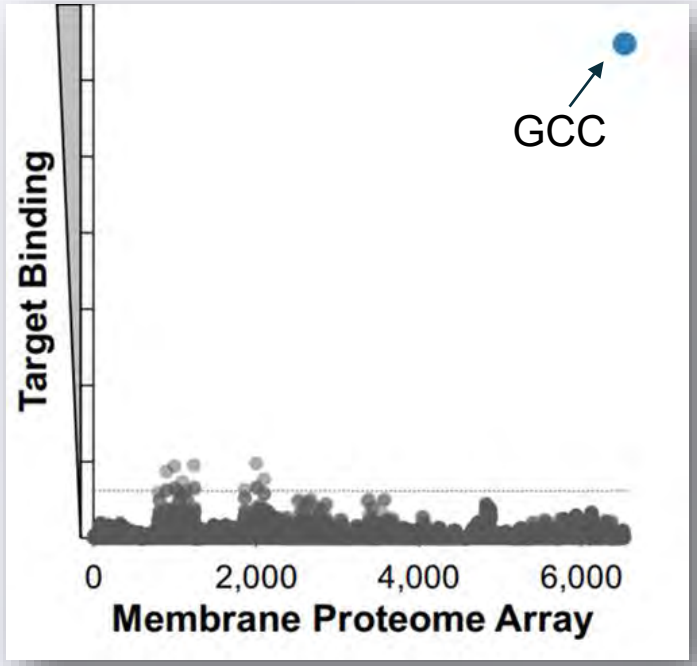
LCAR-G08 VHH Binder Characterization *in vitro*

- Humanized sdAb with high affinity and specificity
- No off-target binding in membrane protein array

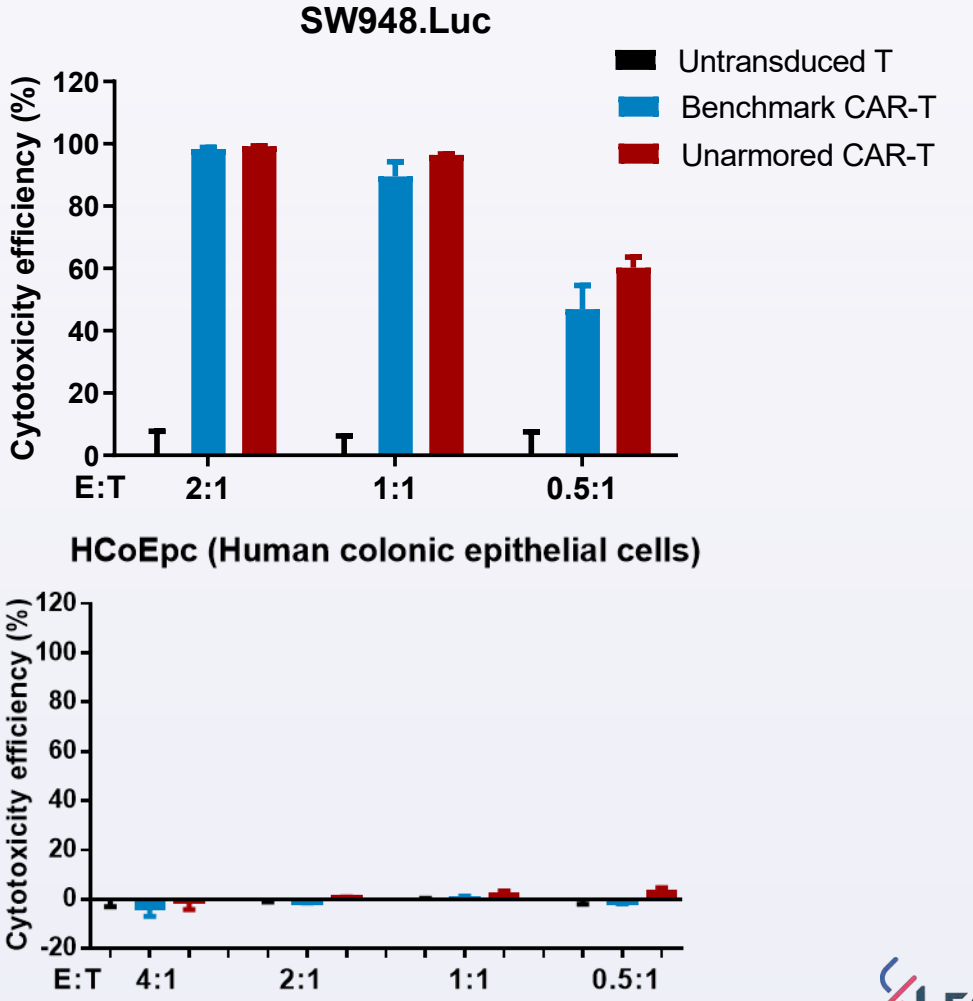
Binding affinity by SPR

Antibody	ka (1/Ms)	kd (1/s)	KD (M)
VHH binder	1.27E+05	1.29E-04	1.02E-09
Benchmark	9.38E+04	1.30E-03	1.38E-08

Membrane Proteome Array



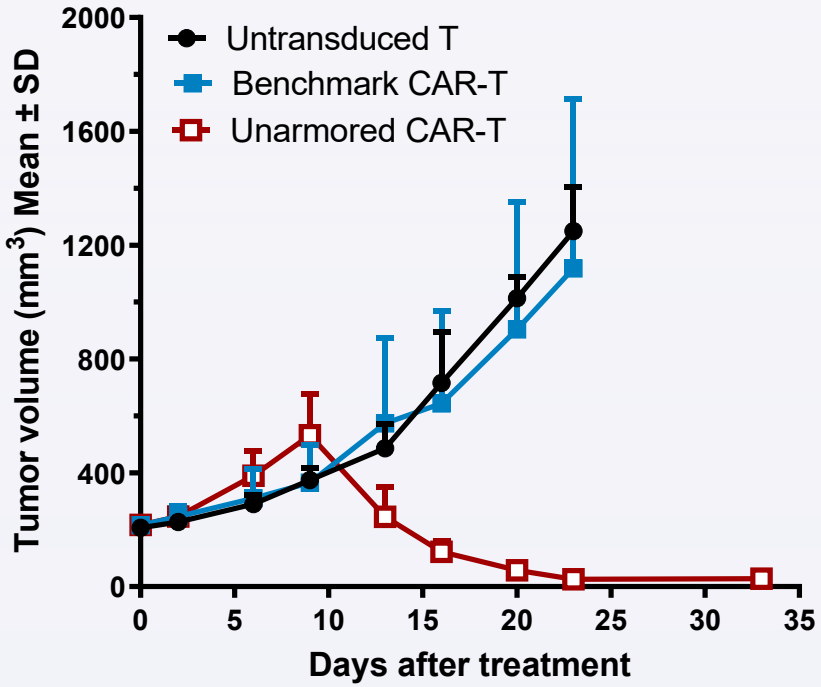
- LCAR-G08 (unarmored CAR-T) elicited cytotoxicity on CRC cells, but not on normal primary colonic cells (HcoEpc)



LCAR-G08 VHH Binder Characterization *in vivo*

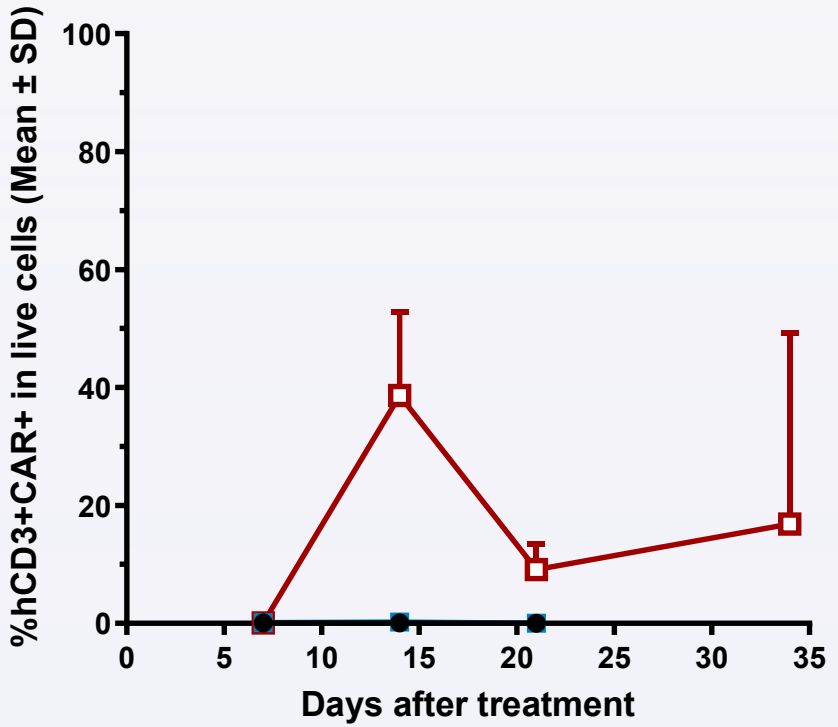
- LCAR-G08 (unarmored CAR-T) exhibited better efficacy and T cell expansion than benchmark at low dose *in vivo*.

Tumor Control Efficacy



(SW948 subcutaneous tumor, 0.3M CAR-T)

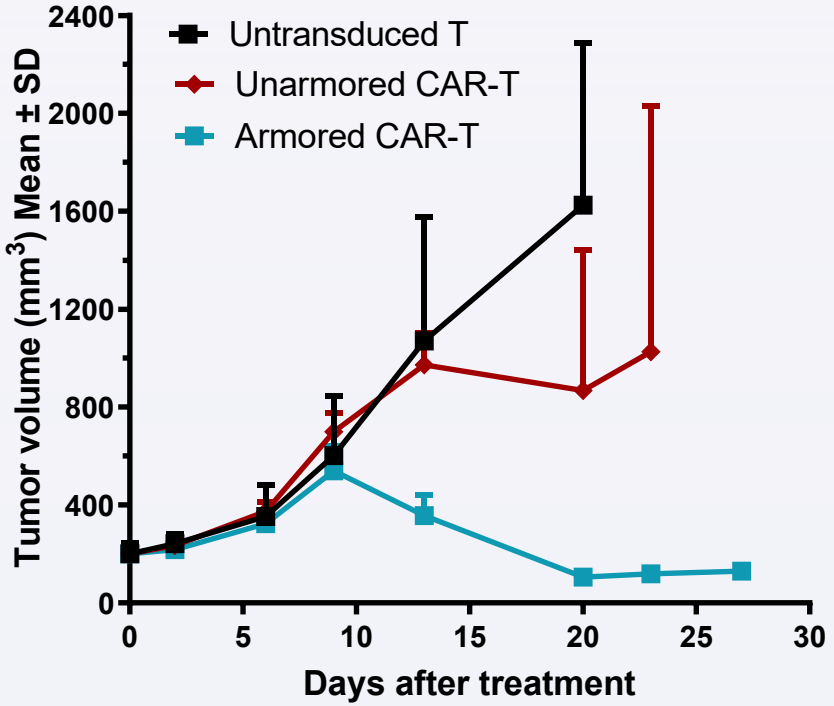
CAR-T Expansion Kinetics



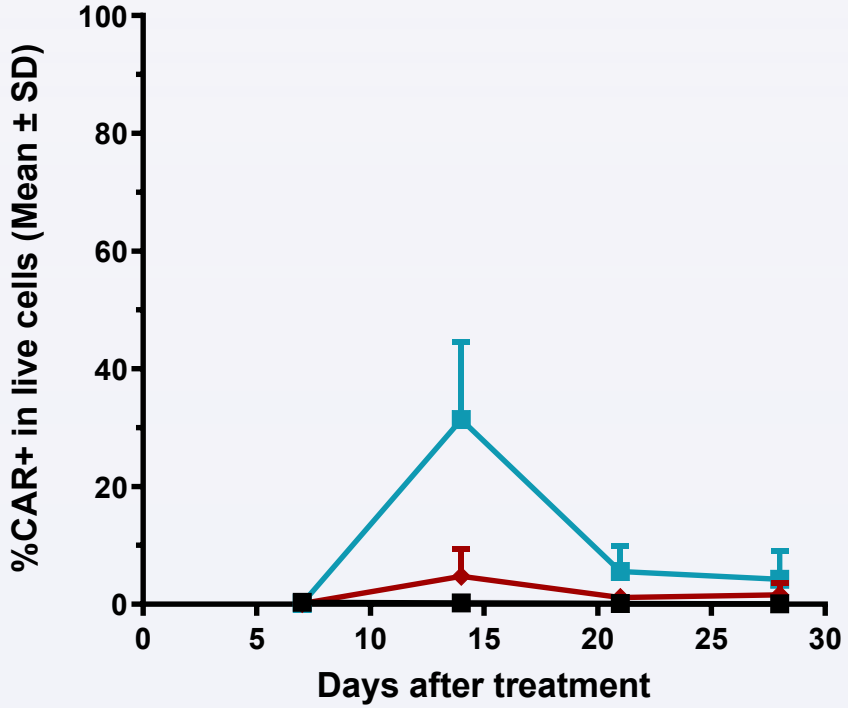
Legend's Armor Markedly Improves CAR-T Function

- LCAR-G08T is armored with a membrane bound receptor converting TME immunosuppressive signal to an activation signal.
- Armor enhances CAR-T anti-tumor efficacy *in vivo* at low dose of 0.1M CAR-T in the LS1034 subcutaneous tumor model.

Tumor Control Efficacy

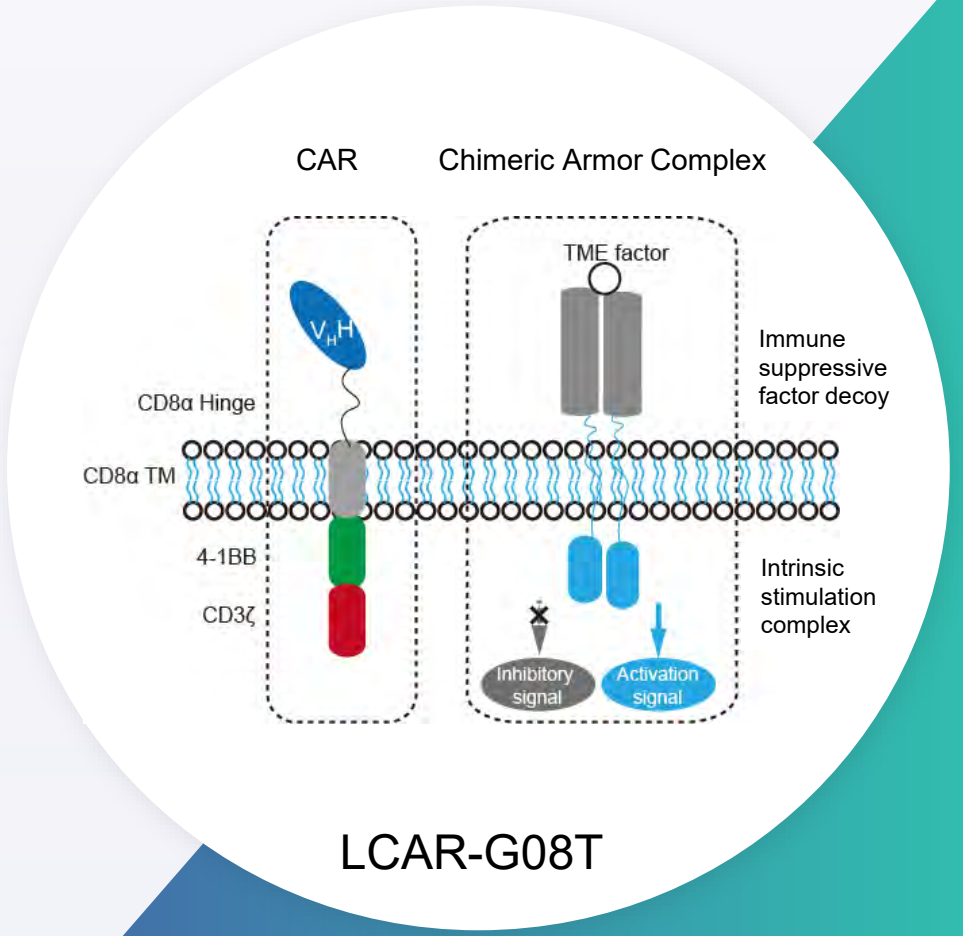


CAR-T Expansion Kinetics



Conclusion: LCAR-G08T

- GCC is a promising target for CRC and other gastrointestinal cancers.
- Humanized sdAb-derived binder with high GCC binding affinity, specificity.
- Innovative armor improves CAR-T persistence and overcomes immunosuppressive TME in a preclinical model.
- First-in-human study in preparation.



Allogeneic Platform

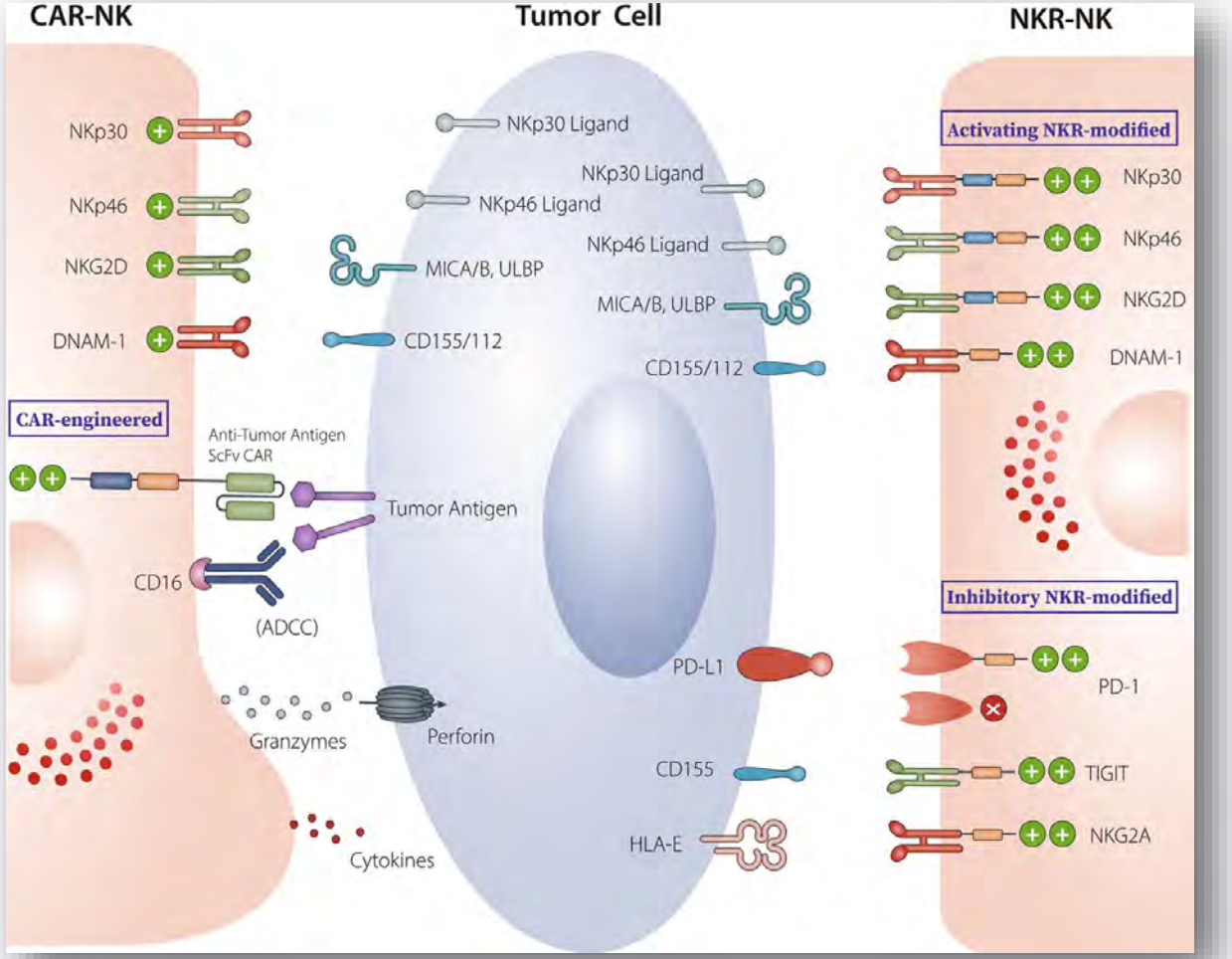
CAR-NK

Solid Tumors

Allogeneic Platforms

CAR-NK Immunotherapy

- NK cells are fast and serial killer of cancer cells
- CAR-NK offers multiple cytotoxicity MOAs:
  - CAR independent killing (e.g. NKG2D, NCRs, etc.)
  - CAR dependent killing
  - Antibody-mediated ADCC
  - Cytokines to activate host immune response



Zhang, C. et al. Cell Mol Immunol 18, 2083–2100 (2021)

Legend Allogeneic CAR-NK Therapy

CHALLENGES

- Short persistence of NK cells
- Multiple dosing required
- Low transduction efficiency
- Difficulty with cryopreservation
- HvG rejection

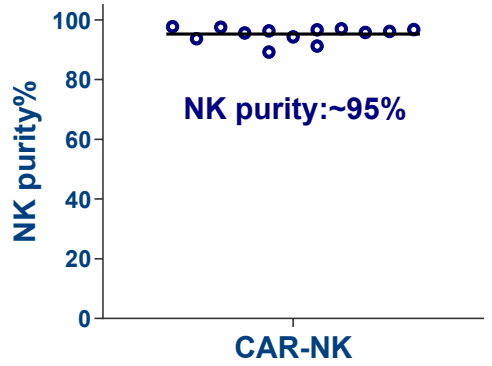
LEGEND BIOTECH

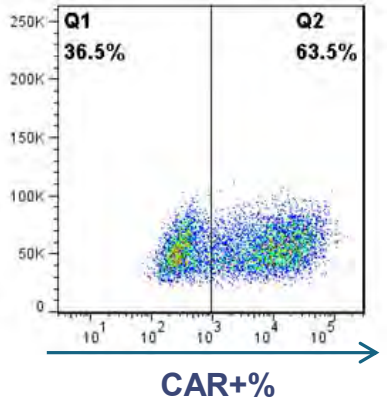
- Long term tumor regression by single low dose of LGkine armoring CAR-NK in animal models
- Robust transduction efficiency
- Cryopreserved product maintains viability and functionality
- Efficient anti-HvG mechanism to enhance persistence and efficacy

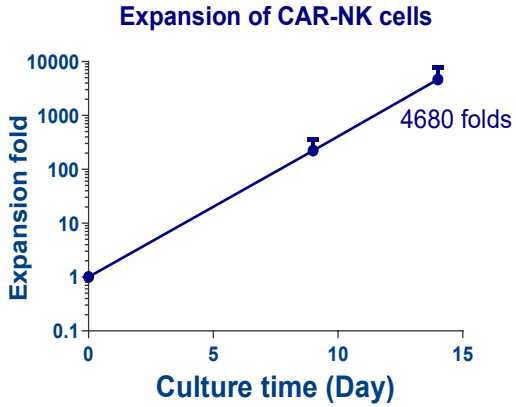
Key Features of Legend CAR-NK Product

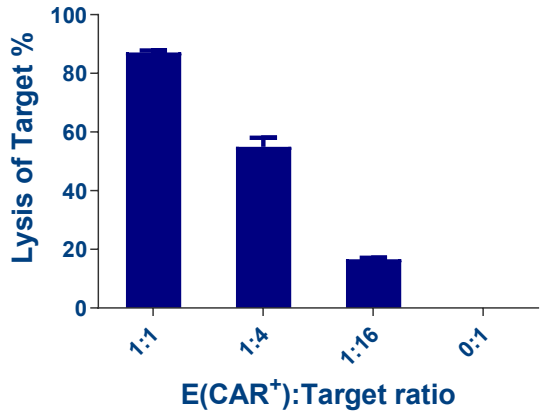
- High purity
- High transduction efficiency

- Robust expansion process
- Strong anti-tumor activity



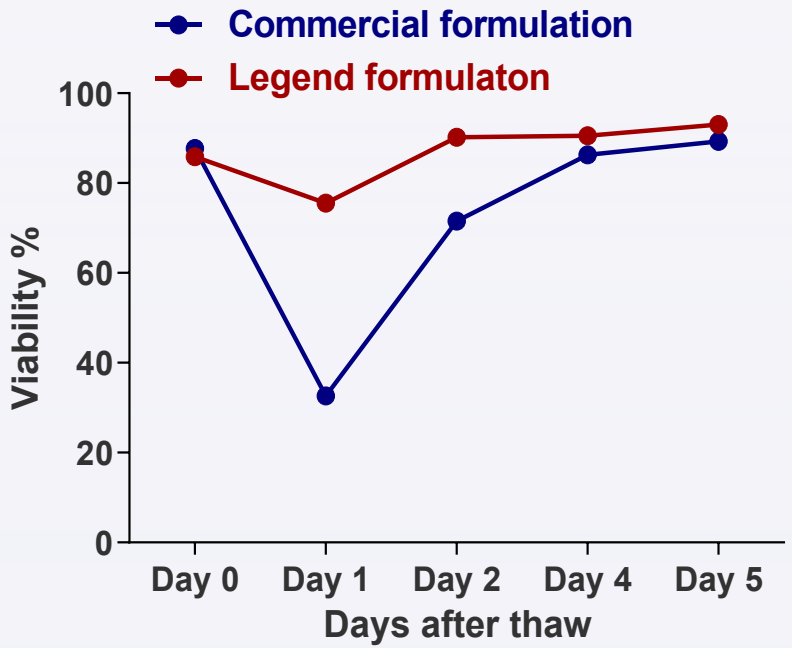




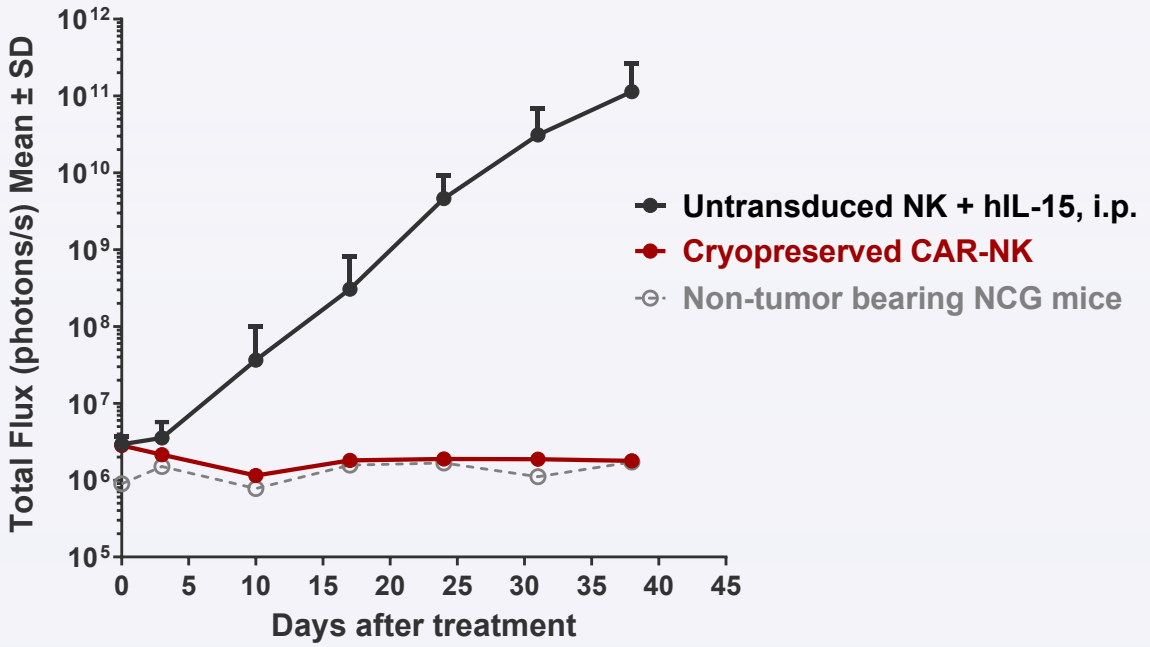


Cryopreserved Legend CAR NK Product Maintains Viability and Functionality

Viability of Cryopreserved Product in vitro

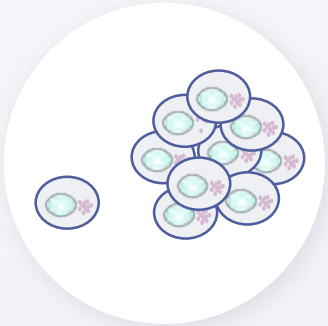


Anti-Tumor Efficacy of Cryopreserved Product in vivo



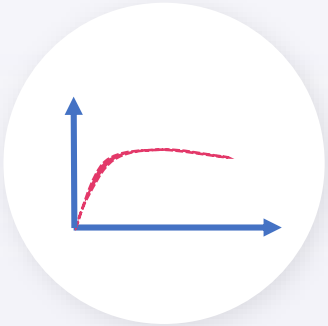
Highlights of Legend's CAR-NK Product

CMC



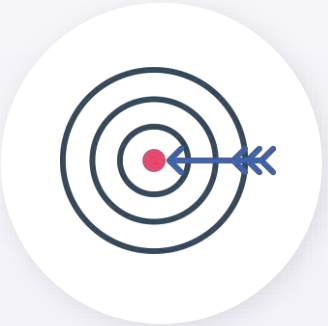
- High transduction efficiency and purity
- >500 doses/leukopack (assuming 300M/dose)
- Optimized cryopreservation maintains viability and functionality

Efficacy and persistency



- Potent and long-term anti-tumor efficacy across multiple tumor models
- Strong IP position

Tumor targeting



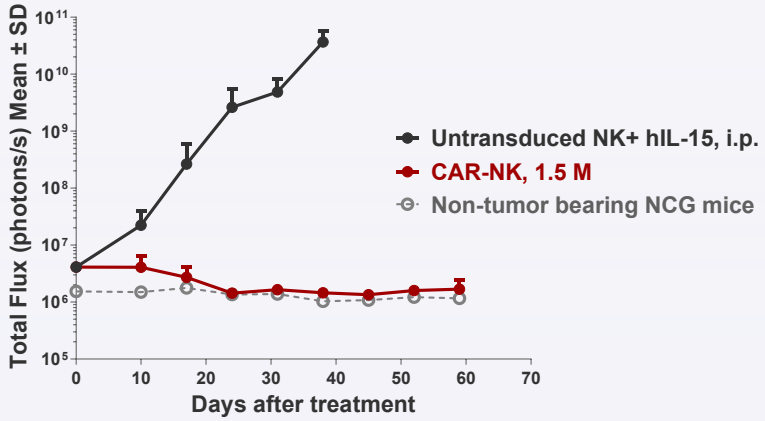
- Bi-paratopic binders to enhance immune synapses
- Optimized CAR signaling domain for NK activation
- Synergistic effect when combined with mAb

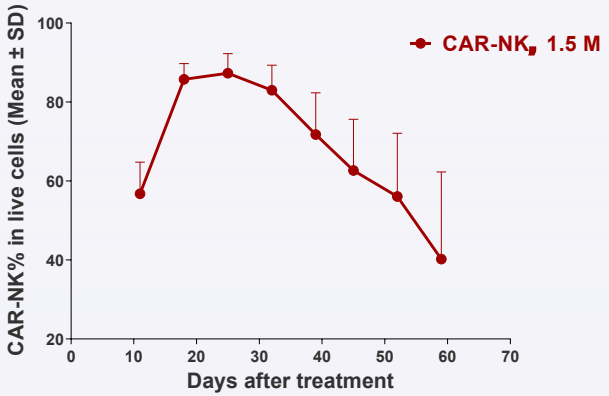
HvG solution

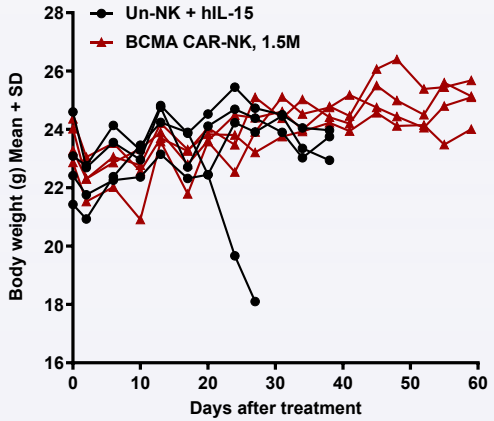
- Strong proliferation to off-set HvG rejection
- IP protected HvG strategies to further enhance CAR-NK persistence and efficacy in preclinical models

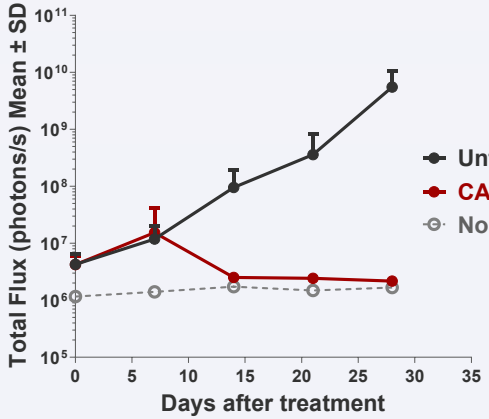
Preclinical CAR-NK Efficacy and Safety Profile at Low Dose Treatment

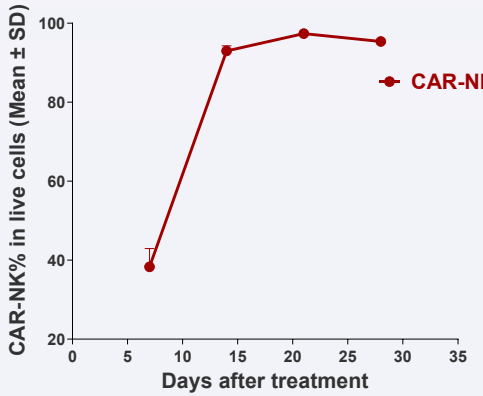
- Complete & durable tumor regression by a single low dose (0.5 M or 1.5 M) in preclinical *in vivo* models
- No sign of body weight loss



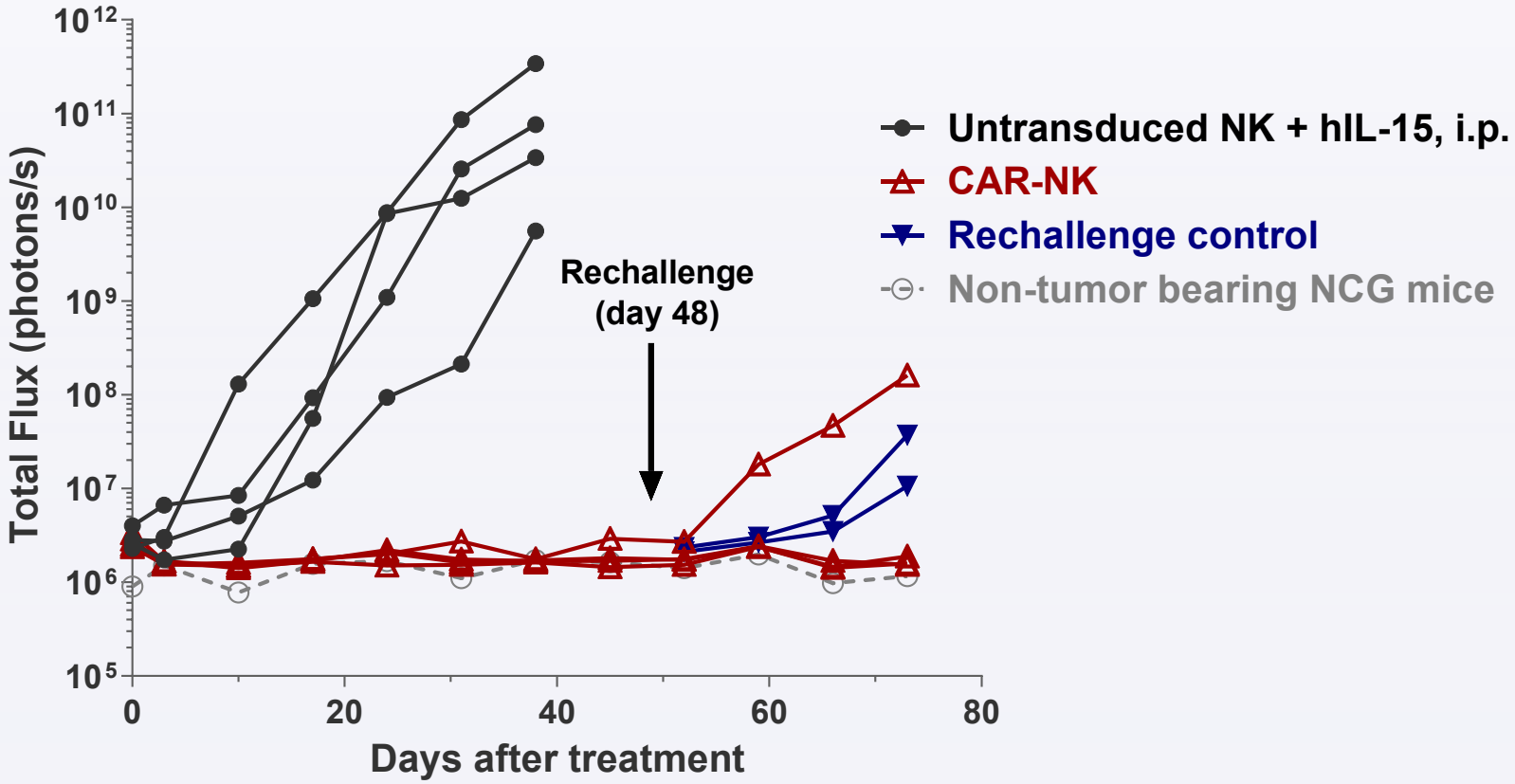








Durable Protection Upon Tumor Rechallenge



- Three out of four animals maintained complete tumor regression after re-challenge of tumor cells until the end of the experiment (each line represents one animal)
- No sign of body weight loss was observed during the study

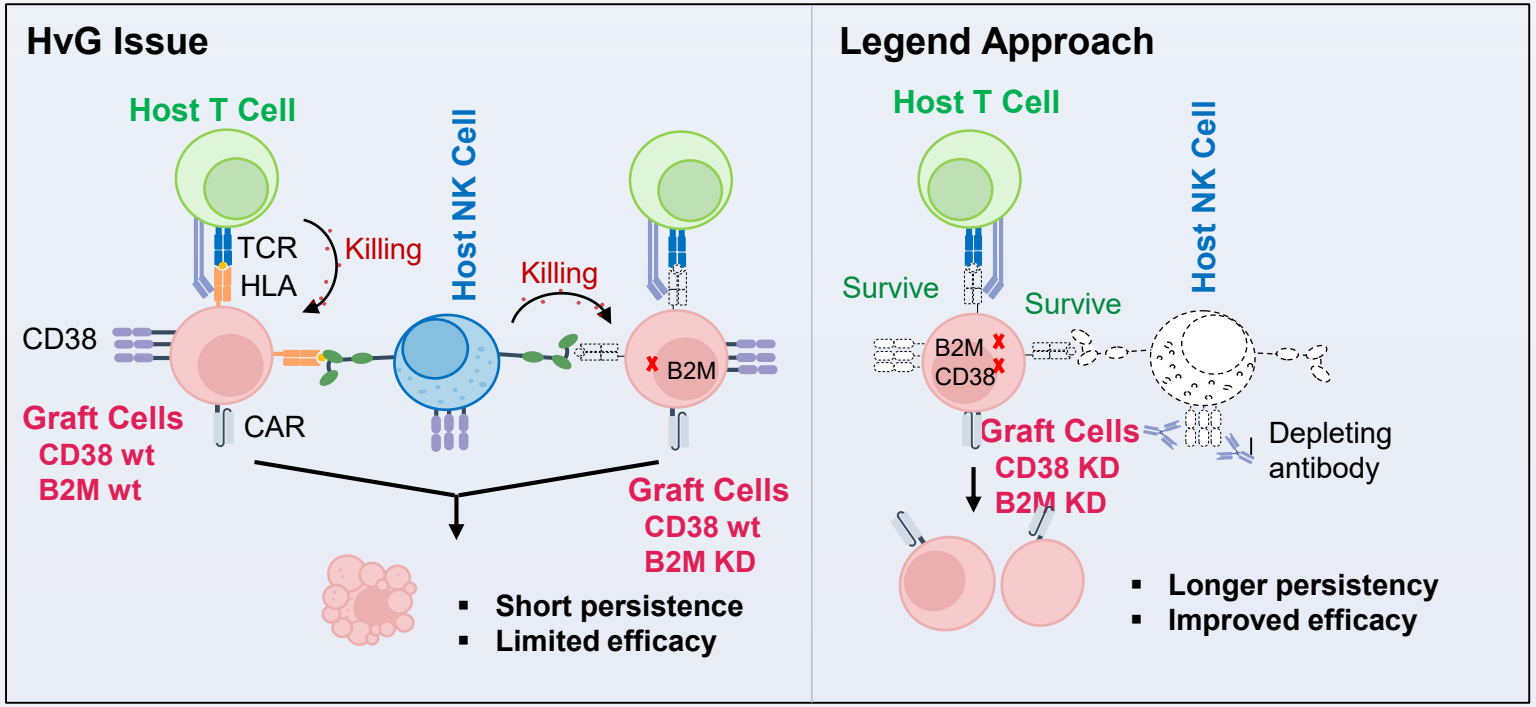
HvG Strategy

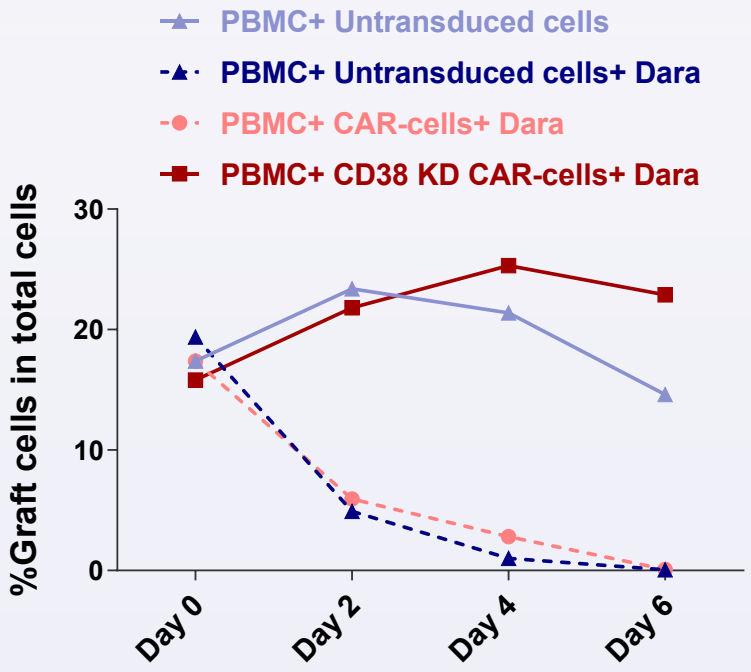
Approach

- B2M knock down (KD) to avoid host T recognition
- CD38 KD to avoid CD38 antibody fratricide
- Treatment with CD38 mAb to eliminate host NK cells

Potential Benefit

- Avoid recognition by host T and NK cells
- Simple CMC process: single vector to express CAR module with B2M KD and CD38 KD module in one transduction





Summary of Legend CAR-NK Platform

Potency and durability

- Unique armor enables10-30x lower dose to achieve complete tumor regression compared with benchmark in preclinical *in vivo* models
- Prolonged exposure of CAR-NK with single dose (>60 days); Durable control of tumor growth *in vivo*

Safety

- CAR-NK treated animals showed no weight loss

Persistency and HvG solution

- Potent expansion to off-set HvG rejection
- Engineered anti-HvG protection helps extending the persistency of CAR-NK product

CMC

- Product characterized with high viral transduction rate and high NK purity
- Product with enhanced metabolic fitness and less exhaustion phenotype
- Capacity: >500 doses/leukopack (assuming 300M per dose)
- Optimized cryopreservation process maintains cell viability and functionality

Allogeneic Platform

CAR-γδ T

Solid Tumors

Allogeneic Platforms

γδ T Cells As Next Generation Cancer Cell Therapies

Efficacy

- Express T-cell and NK cell receptors, facilitating adaptive and innate anti-tumor activities to address target heterogeneity
- Infiltrate to most hematologic malignancies and solid tumors
- Presence of γδ T cells in tumors strongly correlates with improved overall prognosis, survival and PFS

Safety

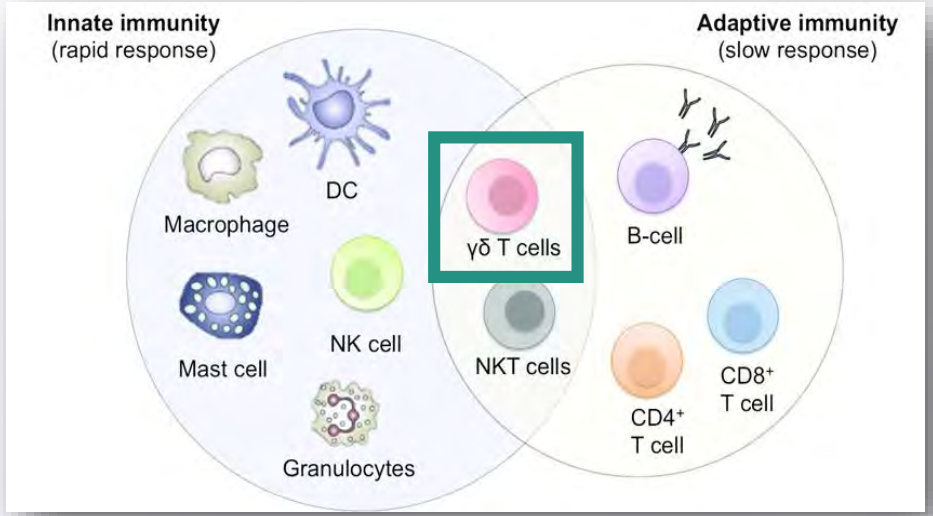
- γδ T cells naturally do not cause GvHD

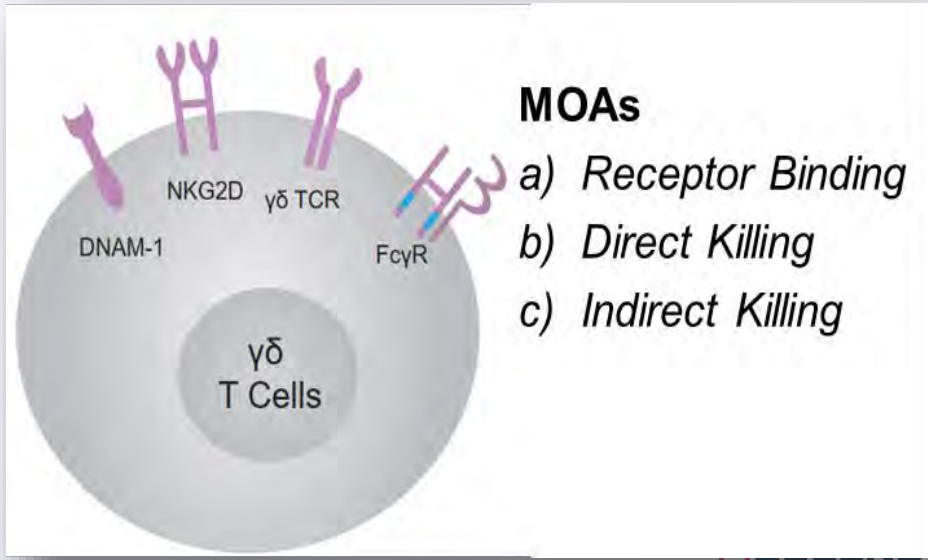
Manufacturing

- Healthy donor derived
- Can be robustly expanded in a GMP-compliant manner
- Can be effectively redirected using CAR constructs

Hurdles

- No cytokine secreted to support γδ T proliferation after activation
- Potential allo-rejection by host immune cells



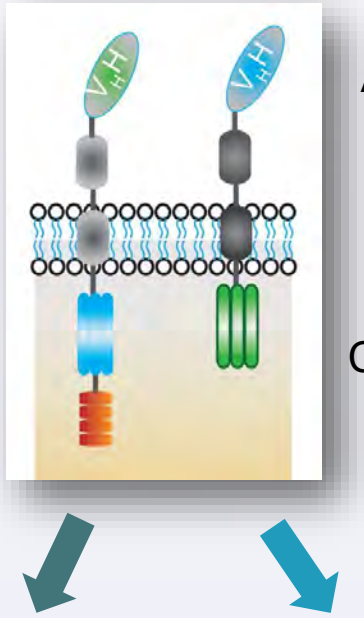


Innate Armor CAR-γδ T Platform

Mimicking natural co-stimulatory signaling in CAR-γδ T cells

Antigen binding domain 1

Antigen binding domain 2



Signaling from adaptive immunity

Co-signaling from innate immunity

Activation and cytotoxicity

Cytokine secretion and cell expansion

- Potent & selective cytotoxicity
- Robust cell expansion/persistence
- Low cytokine secretion

Robust Scalable Manufacturing Process


Donor Screening


Apheresis


PBMC Isolation


CAR-γδ T Expansion


αβ T cell Depletion


Formulation & Cryo Storage

- Leverage our expertise and capabilities with autologous CAR-αβ T production
- *Feeder free, serum free, fully closed and semi-automated* CAR-γδ with consistency and scalability
- Cost efficient: 1 leukopak for 1000 doses#

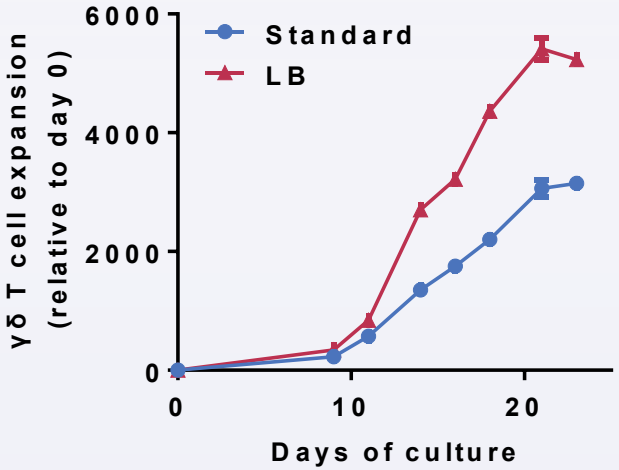
**: tested on three hematological and one solid tumor model*
 # : current estimate assuming a flat dose of 100M/dose

Metrics	Legend Biotech
Process	10-15 days
Cell fitness	>90% Tcm
Exhaustion marker	Low PD-1 and TIGIT expression

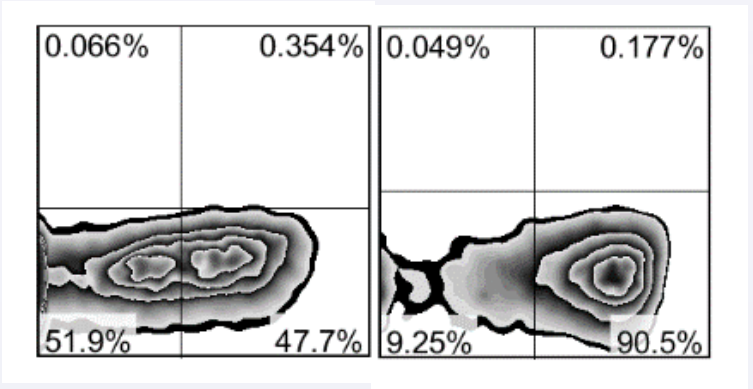
Our Manufacturing Process Leads to Differentiated Product

Better Expansion and Improved T Cell Fitness

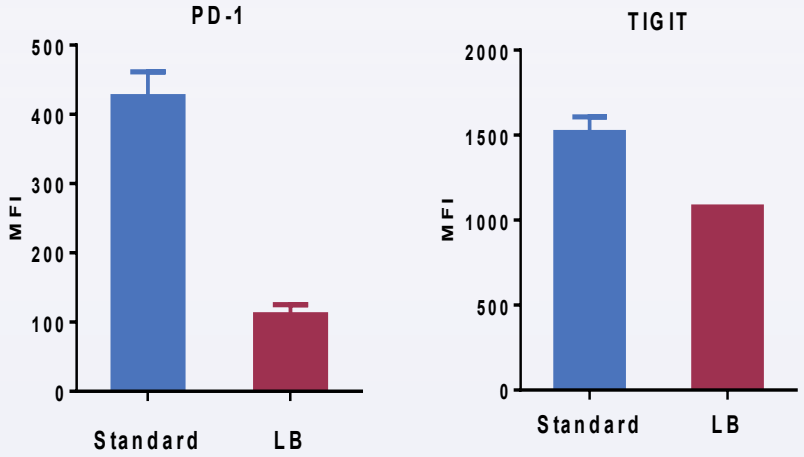
Expansion



Standard *Legend Biotech*



Exhaustion marker



Standard: *competitor CMC*
LB*: Legend CMC*

Allogeneic Program

LB2103

Solid Tumors

Allogeneic Platforms

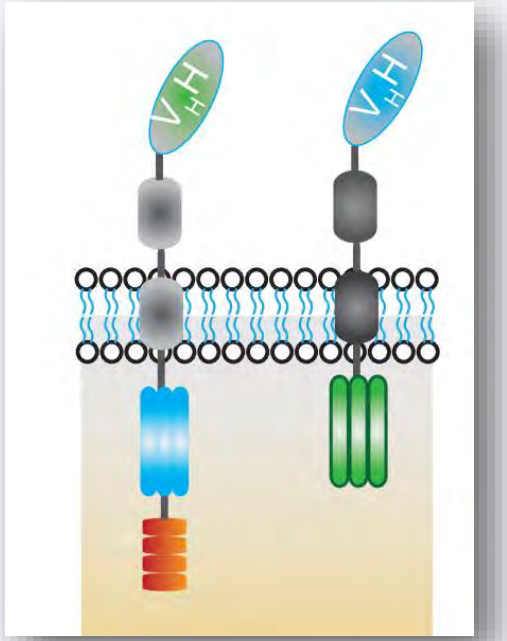
LB2103: BCMA-targeting CAR-γδ T Cell for Multiple Myeloma

TARGET

- BCMA: highly expressed in myeloma cells
- No expression in normal tissues beyond B cells

MOA/SCIENTIFIC RATIONALE

- Two VHHs bind to BCMA with high affinity;
- Innate armor to increase cell proliferation and cytotoxicity upon antigen engagement



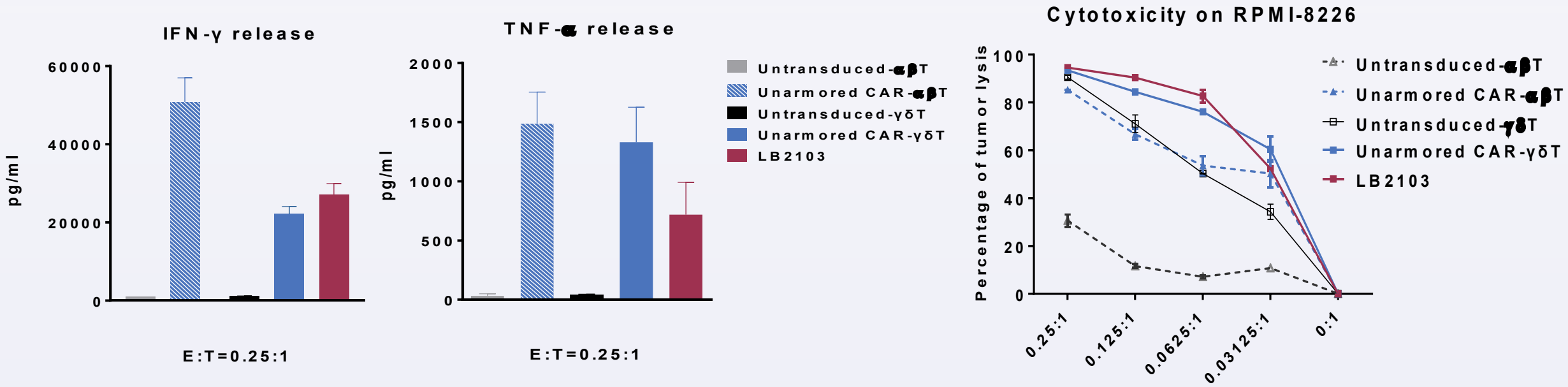
CLINICAL DEVELOPMENT STRATEGY

- Well-tolerated *in vivo* in xenograft models
- China IIT ongoing

1 Danaee H et al PLoS One, 2017, 12(12): e0189953.
2 Magee M S, et al. Oncoimmunology, 2016, 5(10): e1227897.

LB2103 Releases Lower Levels of Cytokines Than CAR-αβ T

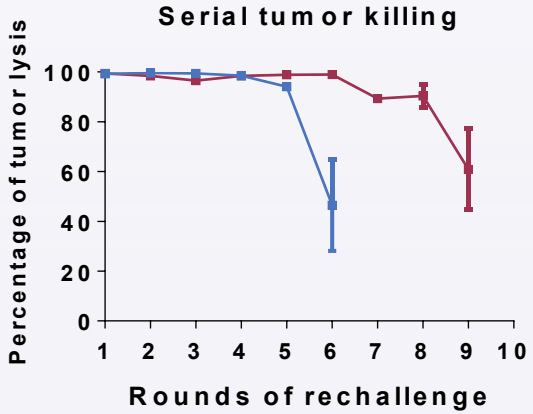
- Lower IFN-γ and TNF-α release from LB2103 than CAR-αβ T
- No detectable IL-6, IL-17, IL-8, IL-1β from LB2103
- Higher cytotoxicity from LB2103 than CAR-αβ T

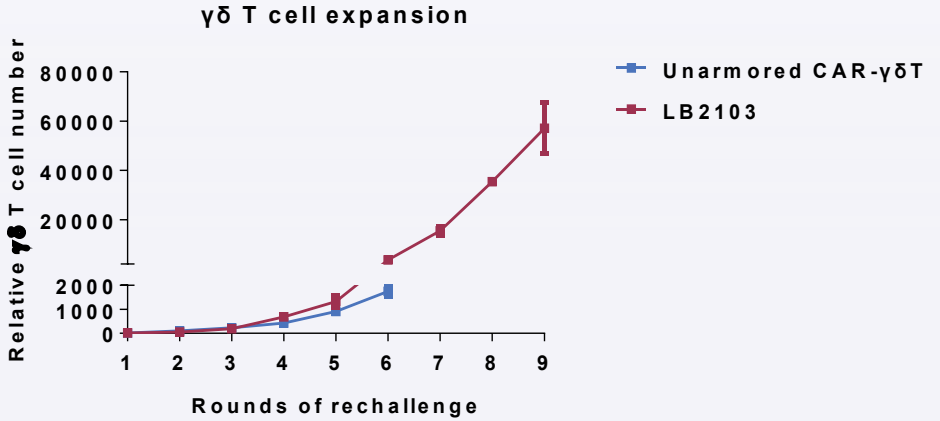


LB2103 Exhibits Enhanced Cell Expansion and Potency

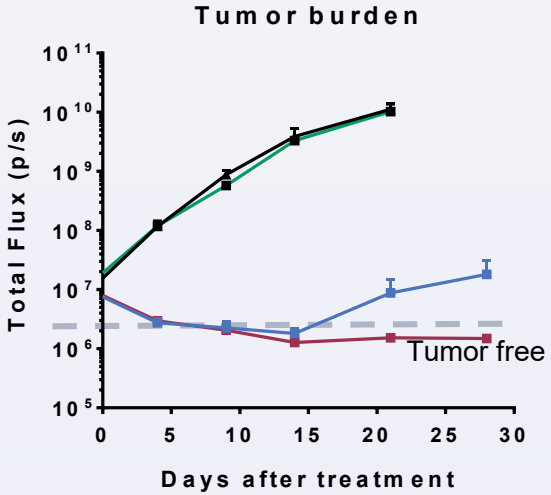
- LB2103 had better potency and proliferation than unarmored CAR-γδ T in repetitive tumor killing assay
- LB2103 exhibited better tumor control than unarmored CAR-γδ T *in vivo*

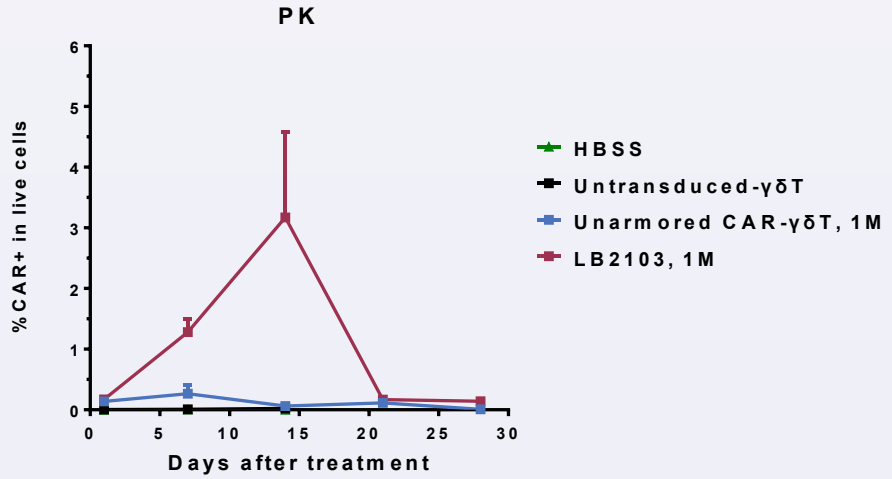
In vitro





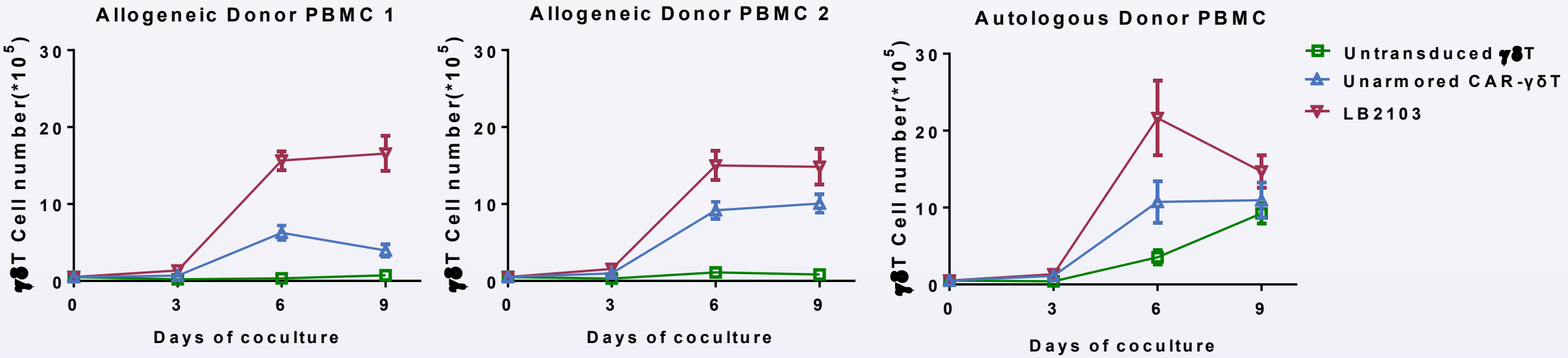
In vivo





LB2103 Exhibits Decreased HvG Potential

Improved persistence of LB2103 over unarmored CAR-γδ T in the presence of allogeneic PBMC



CAR-γδT : PBMC : tumor = 1:30:1

- Legend has IP-protected approaches to address HvG that can be incorporated to LB2103

Summary of Allogeneic CAR-γδ T with Innate Armor

Efficacy

- Potent cytotoxicity with multiple MOAs: CAR-dependent and independent cytotoxicity
- Innate Armor platform with strong IP position
  - Unique armor mechanism to increase CAR-γδ T expansion and persistence

Safety

- γδ T cells naturally do not cause graft-versus-host disease (GvHD)
- Innate Armor platform
  - Tumor antigen-dependent CAR-γδ T expansion
  - Lower levels of pro-inflammatory cytokines secreted compared to CAR-αβ T cells

CMC

- Feeder free, serum free, closed, and semi-automated manufacturing process with consistency and scalability
- Proprietary process that enriches central memory γδ T cells and improves γδ T cell fitness
- Currently estimating >1000 doses per leukopak

Clinical Development Strategy

- First-In-Human study in China ongoing for clinical POC

Global R&D Strategy

Institutional R&D Model that accelerates Cell Therapy Discovery and Development

People: >300 employees
One of the largest global cell therapy R&D teams

Science: Global
innovation
development
US, China, Europe

Patients: Potential **first/best-in-class** proprietary technology platforms

IP: Strong intellectual property position

CLINICAL DEVELOPMENT

Clinical programs in US

Clinical programs in China

CORE TECHNOLOGIES

CAR-T

NK

γδ - T

PRODUCT PLATFORMS

Autologous

Allogeneic

DISEASE AREAS

Hematologic malignancies

Solid tumors

Q&A

Questions can be submitted by chat or card

LEGEND BIOTECH

Q&A Participants

Ying Huang, Ph.D.
Chief Executive Officer

Guowei Fang, Ph.D.
Senior Vice-President,
Global Head of Research and Early Development

Lida Pacaud, M.D.
Vice-President,
Clinical Development

Steve Gavel
Vice-President,
Commercial Development, US and Europe

THANK YOU