Leading Innovation in Immuno-Oncology

June 2022

Executive Summary

- Clinical stage immuno-oncology company pioneering two novel approaches to engineered cell therapies for the treatment of cancer
  - CAR-CIK platform leverages allogeneic cytokine-induced killer (CIK) cells derived from healthy donor PBMCs
  - Autologous RNA loaded dendritic cell platform

- Lead CAR-CIK program, CMN-005, has demonstrated strong clinical data in hematologic cancers
  - Phase 1/2a data in B-Cell precursor ALL patients: 75% CR rate after a single administration
  - Phase 2 repeat dosing study in ALL ongoing with interim data in mid-2022

- Groundbreaking collaboration with Memorial Sloan Kettering extending CAR-CIK to solid tumors
  - Combines CoImmune technology with proprietary CAR technologies from the labs of David Scheinberg, MD, PhD and Derek Tan, PhD at MSK and Renier J. Brentjens, MD, PhD at Roswell Park
  - Initial pre-clinical proof of concept data from MSK collaboration in 2022

- Lead autologous RNA loaded dendritic cell program, CMN-001, in Phase 2b trial
  - Phase 2b trial in metastatic renal cell carcinoma enrolling with interim data expected in Q2 2023

Management Team

Charles A. Nicolette, PhD
Chief Executive Officer

- Accomplished biopharmaceutical executive with over 25 years of experience in the design, development and clinical testing of immune therapeutics targeting cancer, infectious diseases, and inflammatory/autoimmune diseases.
- Responsible for developing and directing corporate strategy

Lori R. Harrelson, C.P.A
Chief Financial Officer

- More than 20 years of experience in corporate financial management and strategy; led multiple financings in both private and public company settings
- Responsible for financial strategy and management, investor relations

Irina Y. Tcherepanova, PhD
Chief Operating Officer

- More than 20 years of experience in developing and the manufacturing of cellular therapies with a broad understanding of drug development
- Responsible for all aspects of operations including manufacturing, supply chain management, quality control, facilities, IND development and program management

Sukwoo Jeffrey Oh, J.D.
Chief Business Officer

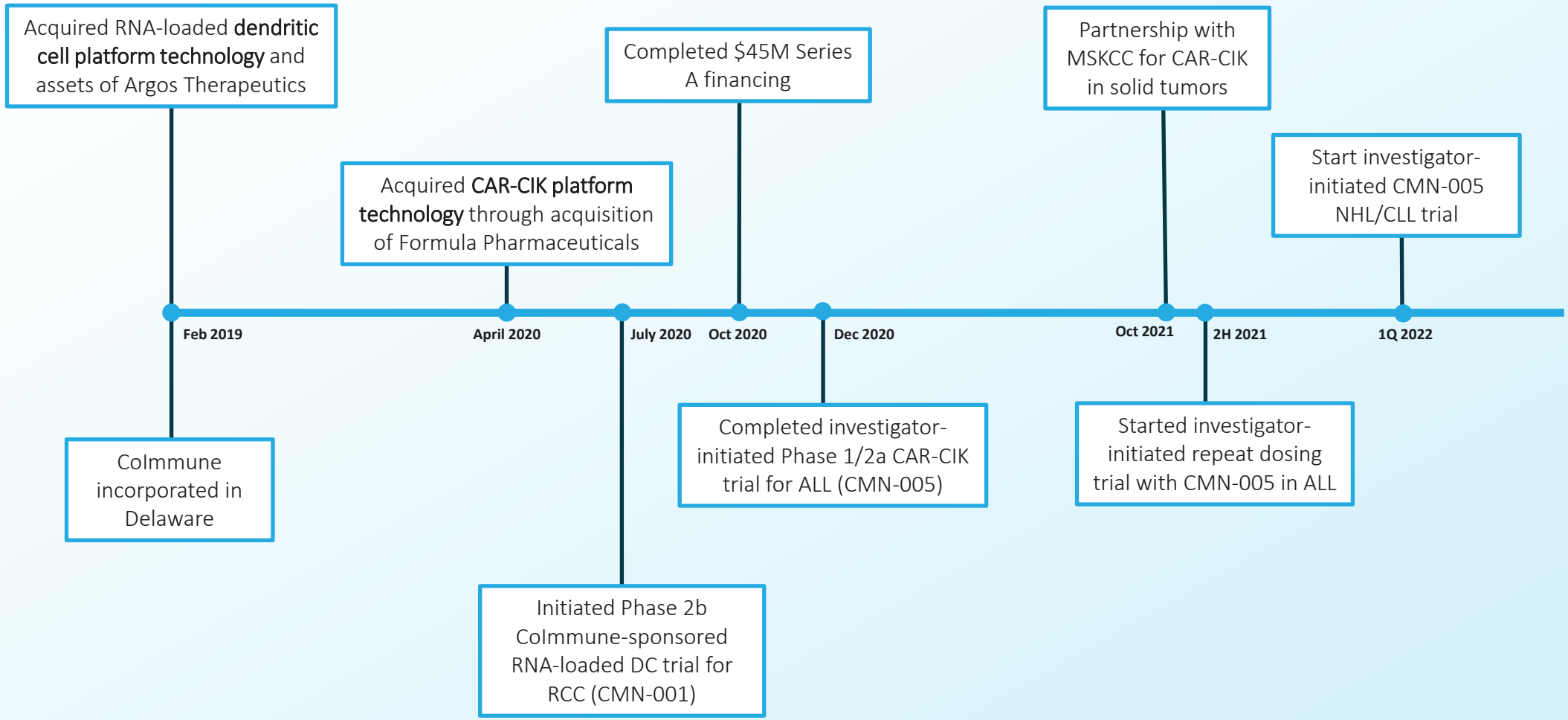
- More than 25 years of experience in business development, strategic and financial roles within the biotechnology industry; has led over 100 licensing and financial transactions
- Responsible for business development and legal affairs

The 14 founding members of CoImmune have worked as a team in cell therapy for >17 years

World-renowned Scientific/Clinical Advisors

Name	Affiliation	Title
Andrea Biondi, MD		Tettamanti Research Center, Department of Pediatrics, University of Milano-Bicocca, Monza, Italy
Alessandro Rambaldi, MD		Director, Department of hematology, Azienda Ospedaliera Papa Giovanni XXIII, University of Milan, Prof of Hematology
Robert Negrin, MD		Director of the Bone and Marrow Transplantation Division and Professor of Medicine at Stanford University; Program Leader of the Immunology and Immunotherapy of Cancer Program at the Stanford University Cancer Center, Stanford, CA
David Scheinberg, MD, PhD		Chair, Molecular Pharmacology Program, MSK; Director, Experimental Therapeutics Center; Vincent Astor Chair
Renier J. Brentjens, MD, PhD		Director, Cellular Therapeutics; Associate Chair, Junior Faculty Development, Department of Medicine; *Scientific cofounder of Juno*
Derek Tan, PhD		Chair, Chemical Biology Program, MSKDirector and Professor, Tri-Institutional PhD Program in Chemical Biology
Miguel Perales, MD		Chief, Adult Bone Marrow Transplant Service
Christopher Wood, MD		Professor, Department of Urology, Division of Surgery, The University of Texas MD Anderson Cancer Center, Houston, TX Deputy Chairman, Department of Urology, Division of Surgery, The University of Texas MD Anderson Cancer Center, Houston, TX
Robert Figlin, MD		Deputy Director, Cedars-Sinai Cancer Steven Spielberg Family Chair in Hematology-Oncology Professor, Biomedical Sciences Professor, Medicine

Company History



Robust clinical pipeline

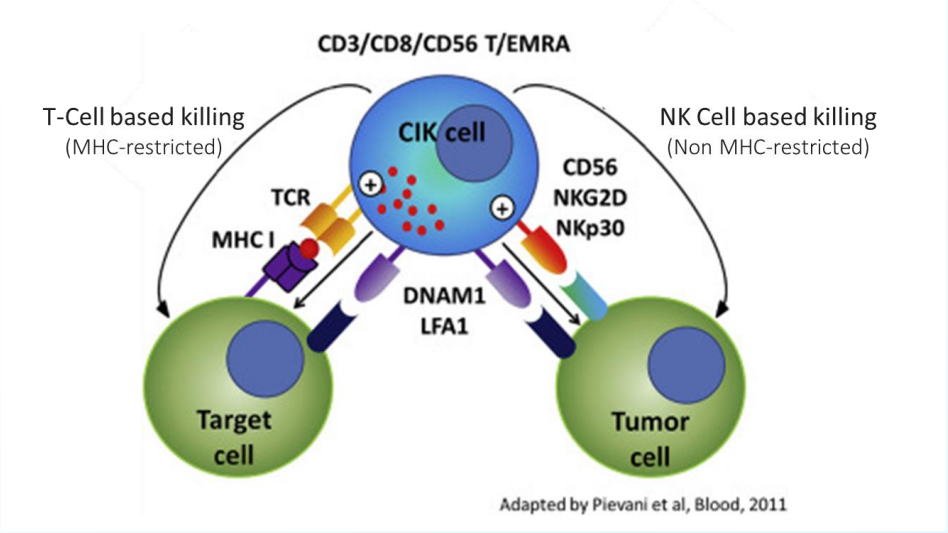
Program	Indication	Pre-clinical	Phase 1	Phase 2	Next Milestone
CARCIK-CD19 (CMN-005) CD19+B cell malignancies	ALL	Dose escalation - Completed enrollment			Final data Publication 1H 2022
	ALL	Repeat dosing - Accruing			Interim data 1H 2022
	ALL	initiate 1H 2022			File corporate IND in 1H 2022
	NHL/CLL	Dose escalation – initiate Q1 2022			IMPD filed; begin accrual Q1 2022
	CLL	initiate 2H 2022			File corporate IND in 2H 2022
CAR-CIK (CMN-006)	AML	Bi-specific CAR			Complete IND enabling studies to file IMPD in Q1 2023
CAR-CIK	Solid tumors	MSK Tech			Proof-of-concept data mid-2022
RNA-loaded DCs (CMN-001)	mRCC	Randomized Controlled phase 2b - Accruing			Interim data Q2 2023

*ALL = Acute Lymphoblastic Leukemia; NHL = Non-Hodgkin's Lymphoma; CLL = Chronic Lymphocytic Leukemia; AML = Acute Myeloid Leukemia; mRCC = Metastatic Renal Cell Carcinoma; MSK= Memorial Sloan Kettering Cancer Center; IST = Investigator sponsored trial (**blue arrows**); CST = Corporate sponsored trial (**black arrows**)

CAR-CIK Platform Technology

Novel CIK cells improve upon NK and T cell approaches

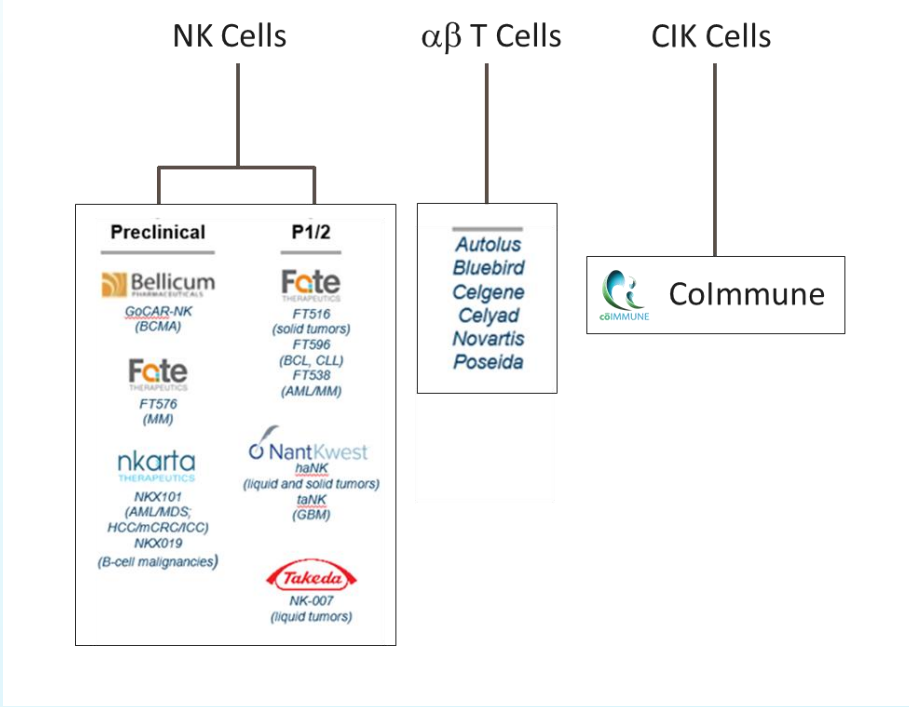
Only cell type that Combines T-cell and NK-cell killing activity*



- CIK cells do not occur naturally in the body
- Strong graft vs. tumor effect with greatly reduced graft vs. host effect compared to T cells**
- Lower toxicity, with no SAEs seen in all 21 patients infused
- Are PD-1 negative

BLOOD (2011) **118**(12):3301
BLOOD* (2008) **112(6):2563

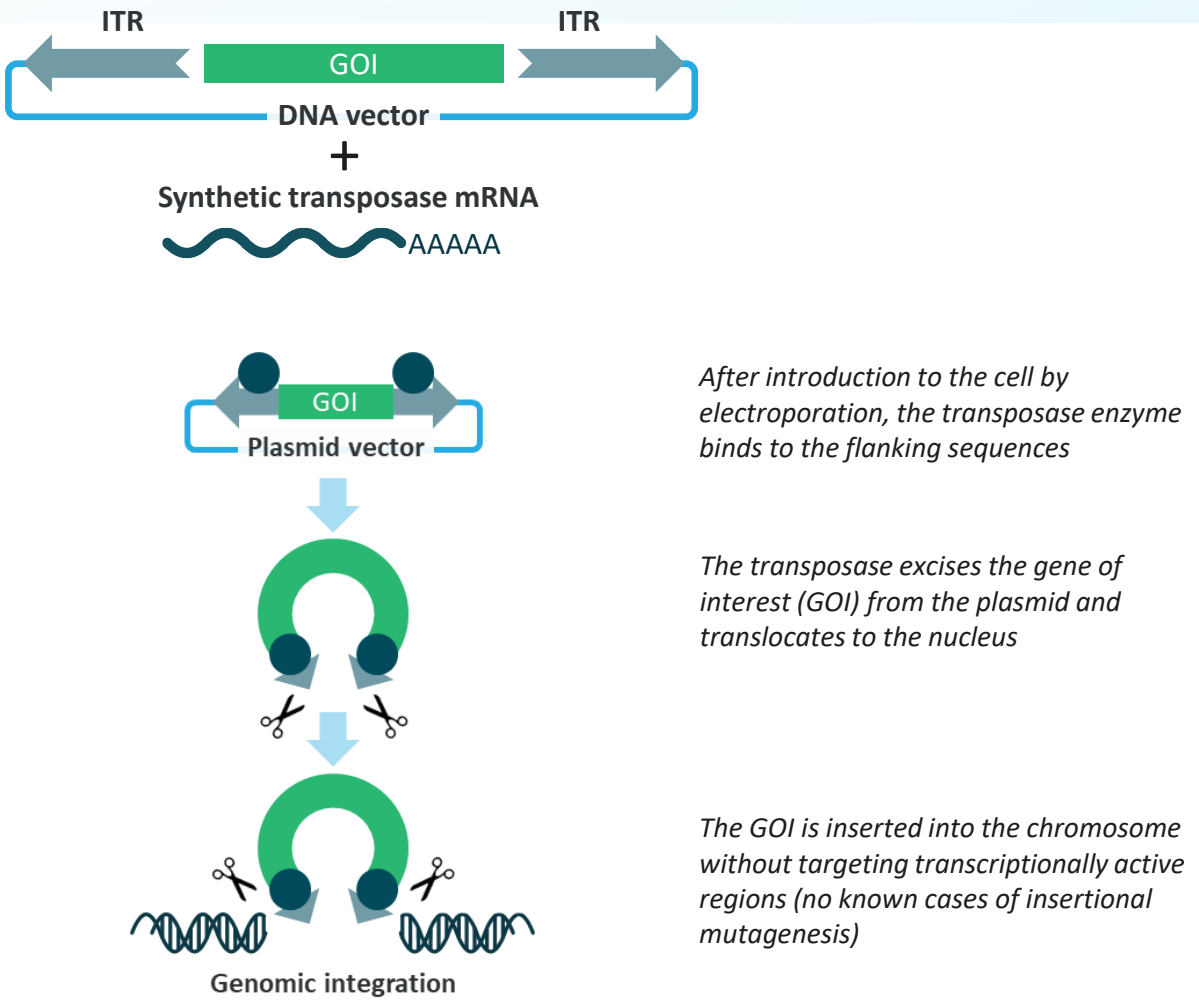
CoImmune is the leader in CIK cell therapy*



*Comprehensive competitive analysis available in e-data room

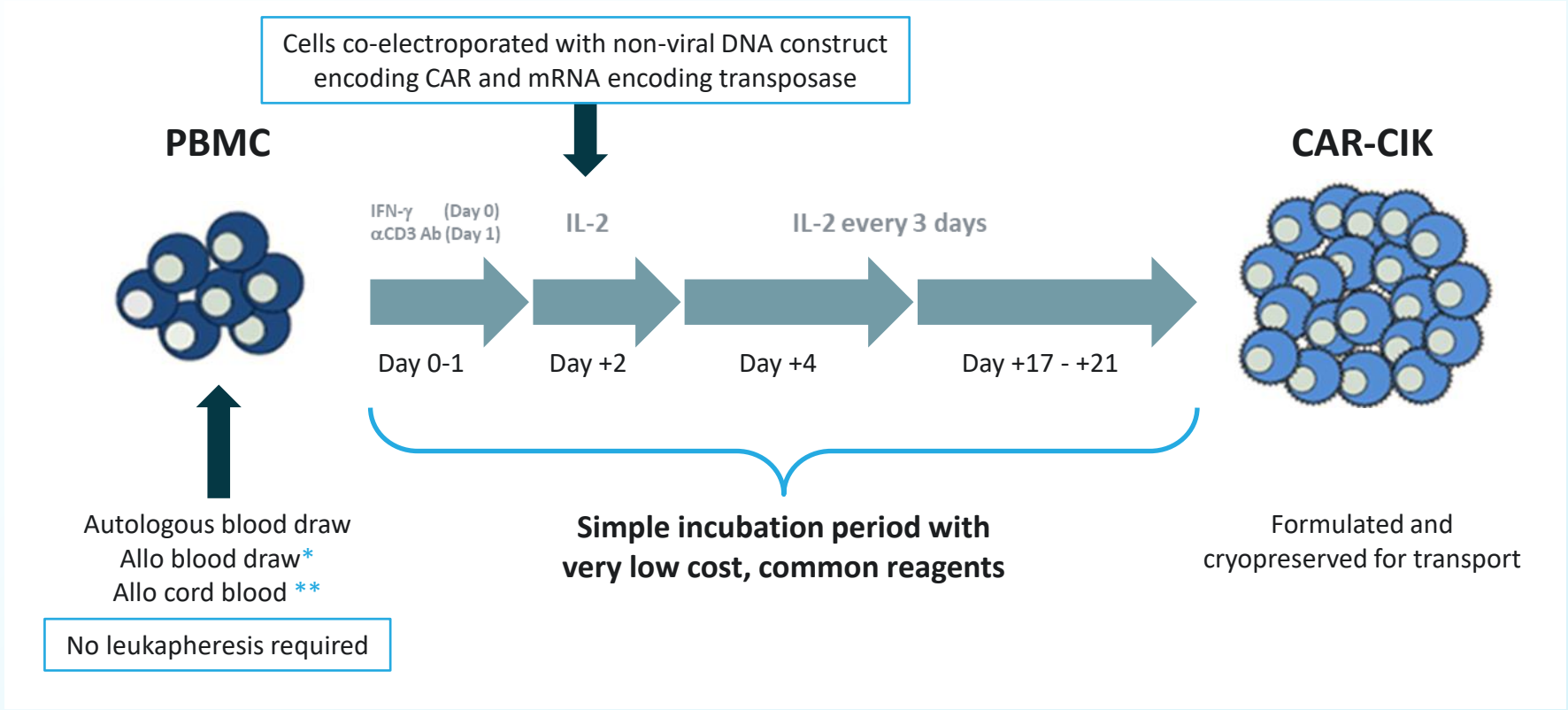
Highly efficient proprietary non-viral gene transfer technology: Sleeping Beauty 100X (SB100X)*

- CoImmune holds exclusive world-wide license
- Simple electroporation step
- Consistently high gene transfer rate (60%-90% genetically modified cells)
- Faster next generation product development timelines achievable with no need for viral stocks



Crit. Rev. in Biochem and Mol Bio (2017) **52**(4):355–380

Streamlined manufacturing process



Production based on material from healthy donors reduces lot-to-lot variability compared to autologous CAR-T therapies

J Clin Invest. (2020) **130**(11):6021-6033
***Bone Marrow Transplant* (2006) **38**(9):621-627

Characterization of CMN-005

CMN-005 Manufacturing Progress

- GMP lot of SB100X RNA manufactured and released
- Stability studies for all intermediate Drug Substance are in progress
- Identified Final Product cryopreservation storage solution logistics
- Completed 8 manufacturing runs (conducted by manufacturing in GMP suites but not GMP material)

Batch	Overall Fold Expansion	% Viability	% CD3+	% CD3+ CD56+	% CD3+ CAR+	Cytotoxicity (% lysis)	VCN (cp/cell)
PreClin-01	345	98	99	52	67	86	2.1
PreClin-02	47	83	97	44	52	92	1.6
PreClin-03	102	90	98	32	77	79	0.7
PreClin-04	138	91	94	64	58	15	0.7
PreClin-05B High	265	78	96	89	82	38	3.8
PreClin-05B Low		86	97	83	80	43	4.0
PreClin-07	316	91	97	53	64	50	0.8
PreClin-08	180	85	98	68	49	43	0.7

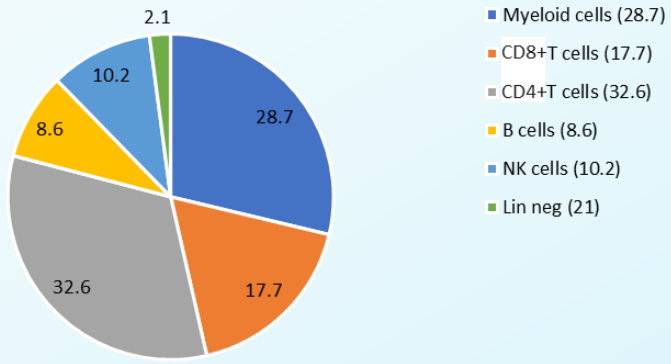
- TCR-vβ analysis complete – demonstrated polyclonal expansion
- Initiated NSG mouse study for efficacy and safety – on-going, but engraftment confirmed
- Integration site analysis by SLiM PCR completed – demonstrated completely random integration
- Developed in-house PCR tests for 5 transplant-associated human viruses (human HHV-6A/B, HHV-7, HHV-8, EBV and B19V)

Initiated the first 2 of 3 GMP runs on April 5th : Required for IND submission

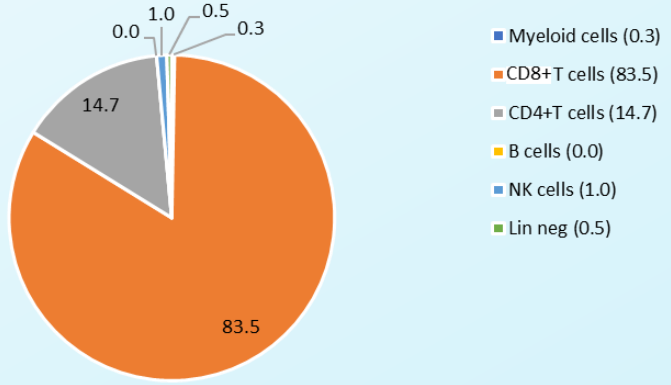
CMN-005: Starting material vs final product

- Monitored CARCIK cell type process impurities during the development and manufacturing process on 8 pre-clinical runs.
- Determination of the percentages of B cells, T cells, myeloid cells and NK cells by multi-color flow cytometry
- Data on the composition of cellular related impurities will be included in regulatory submissions

Day 0 Starting cellular material: mixture of B cells, Myeloid cells, NK cells and T cells



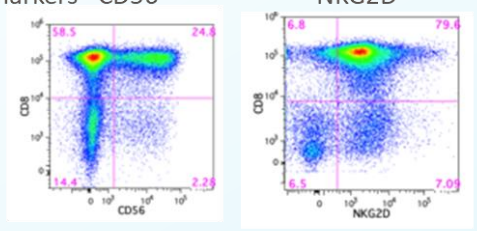
Day 21 Post culture cellular material predominately CD8+ T cells with <2% B cells, Myeloid cells or NK cells



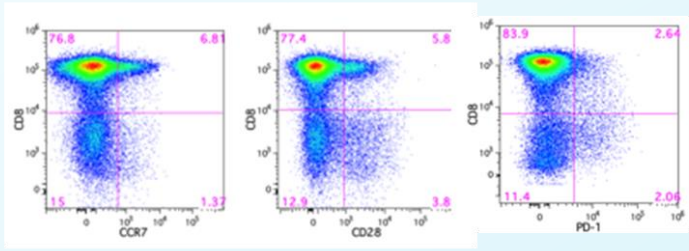
CMN-005 expanded phenotype analysis

- Completed testing of extended phenotype panels during the development and manufacturing process on 8 pre-clinical CARCIK cellular runs
- Characterization of CAR-CIK cells by multi-color flow cytometry defines the unique phenotype of CARIK cells

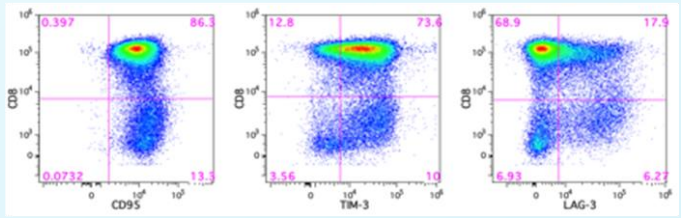
– Expression of NK specific markers CD56 NKG2D



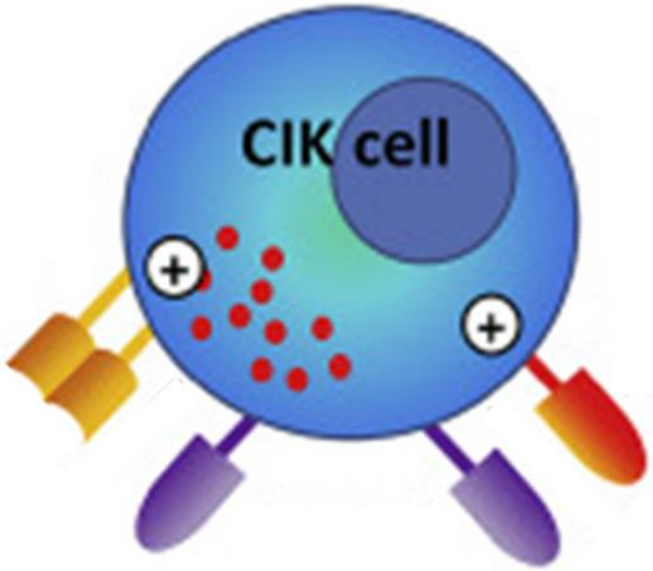
– Lack of T cell markers CCR7 CD28 PD-1



– Early activation/ regulatory markers CD95 TIM-3 LAG-3



CIK cells differ from conventional α/β T cells



Characteristic	Result
↑ NKG2D expression	Allows killing of **antigen loss variants**
↓ CD28 expression	Reduced cytokine secretion, **lowering CRS**
↓ CCR7 expression	Avoids lymphoid organs, **increasing persistence**
↓ homing receptors/chemokines	Don't linger in healthy tissues, **reducing GVHD**

Ideal characteristics to enhance safety and efficacy compared to conventional T cells

Developed an *in vitro* model to detect GVHD (CIK cells vs conventional T cells)

Unrelated random donors (tissue mismatched)

- Donor #1: (HLA-A2$^-$ PBMC – conventional T cells and CAR-CIK cells)
- Donor #2: (HLA-A2$^-$ PBMC – conventional T cells and CAR-CIK cells)

Surrogates for 2 independent Donors

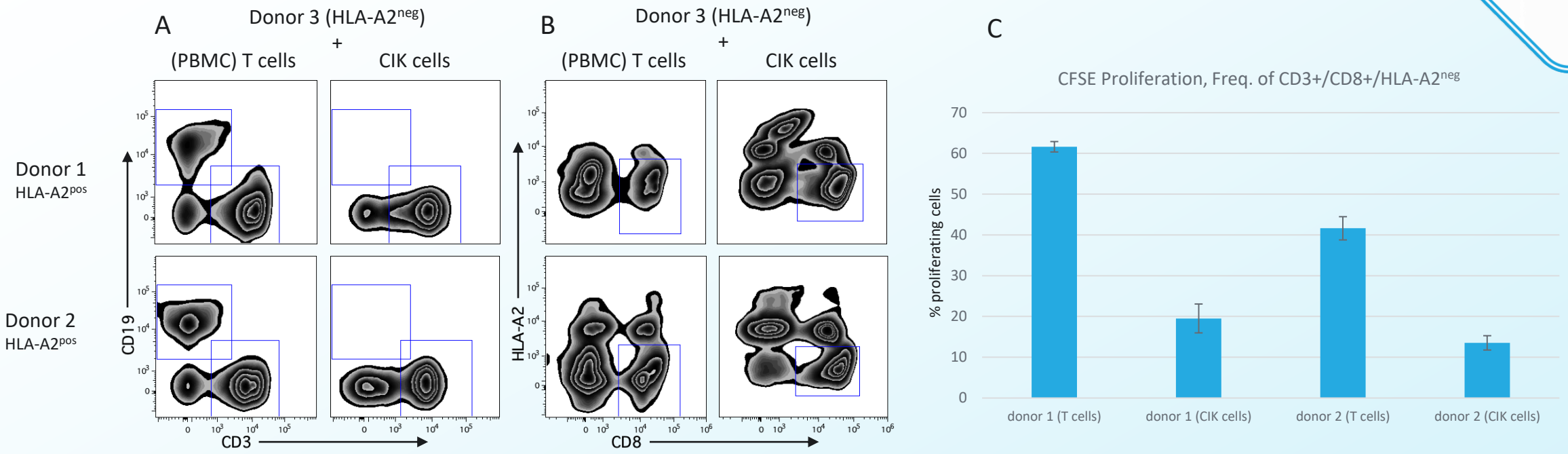
- Donor #3: (HLA-A2$^+$ PBMC)

Surrogate for the patient

Allo mixed lymphocyte reactions

Donor #3 + Donor #1 (Conventional T cells)	Donor #3 + Donor #2 (Conventional T cells)	Donor #3 + Donor #1 (CAR-CIK cells)	Donor #3 + Donor #2 (CAR-CIK cells)
↓	↓	↓	↓
Measure proliferation (surrogate for GVHD)			
↓	↓	↓	↓
Expectation: Strong proliferation High Cytokines	Strong proliferation High Cytokines	Weak proliferation Low Cytokines	Weak proliferation Low Cytokines

In vitro model showing lower allo-reactivity (GVHD) with CIK cells compared to T cells



- Two-way MLR. HLA-A2^{pos} donor PBMCs were co-cultured for 7 days with HLA-A2^{neg} PBMCs or CIK cells generated from 2 different donors.
- B cell killing is evidenced by the lack of CD19 staining only from PBMCs co-cultured with CIK cells (A).
- Gated CD8^{pos}/HLA-A2^{neg} cells (B), show decreased proliferation for cells co-cultured with CIK cells compared to PBMC T cells (C)

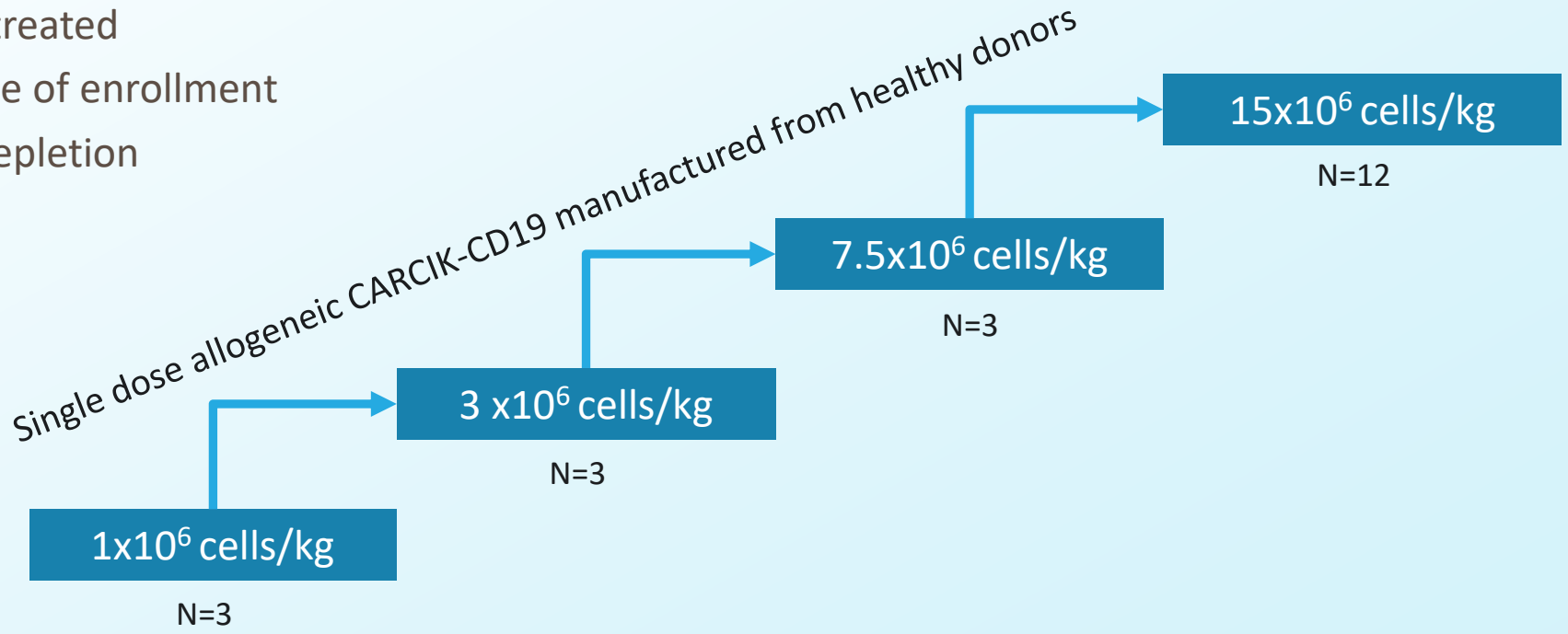
CAR-CIK vs CAR-T

CAR-CIK Products	Approved CAR-T Products
Allogeneic (healthy donors, requires only low-resolution tissue match enabling off-the-shelf availability)	Autologous (complex logistics and supply chain)
Little to no toxicity (allows repeat dosing, no SAEs to date)	Toxicity limits patient eligibility
CIK cells resistant to inducing GVHD	Problems with GVHD and neurotoxicity
Dual killing mechanisms (antigen dependent and independent)	Single killing mechanism (antigen dependent)
Inexpensive non-viral genetic modification (more efficient than virus)	Viral genetic modification significantly increases COGS, potential safety issues
Simplified manufacturing process (multiple doses/run)	No economy of scale

Compared to other allogeneic CAR-Ts under development, CAR-CIK products do not require additional genetic engineering to reduce immunogenicity or immunosuppression of the patient

First ever trial with CAR-modified CIK cells

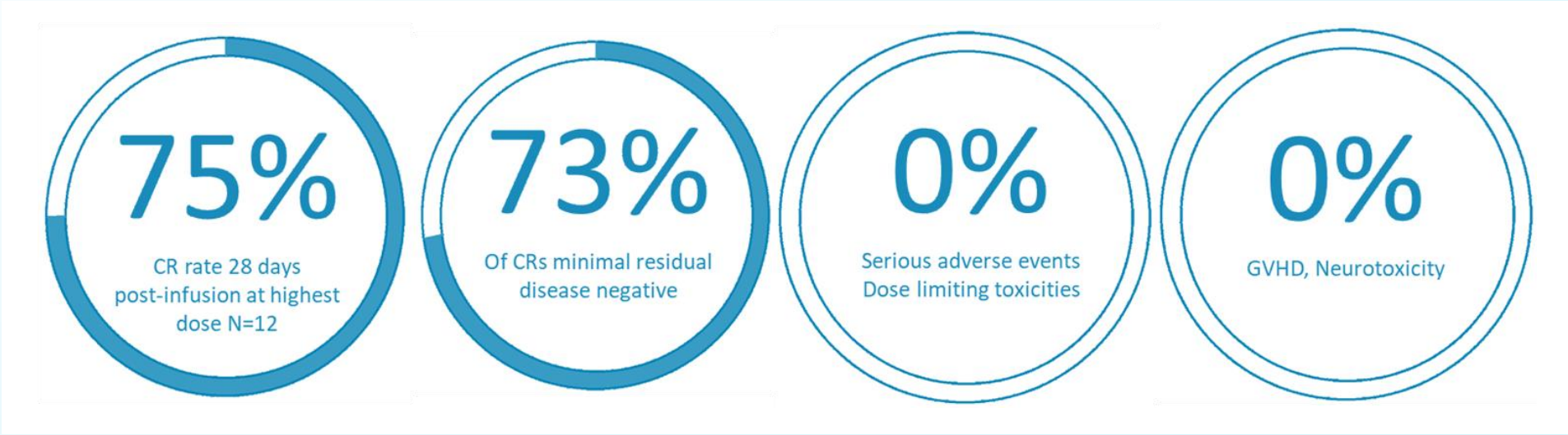
- Phase 1/2a CARCIK-CD19 (CMN-005) dose escalation trial*
- IST trial conducted at 2 sites in Italy
- Adult and pediatric patients with B-cell precursor ALL who are either chemo-refractory or relapsed after allogeneic HSCT
- 4 pediatric/17 adult patients treated
- All patients progressing at time of enrollment
- Single infusion after lymphodepletion
- N=21 evaluable patients



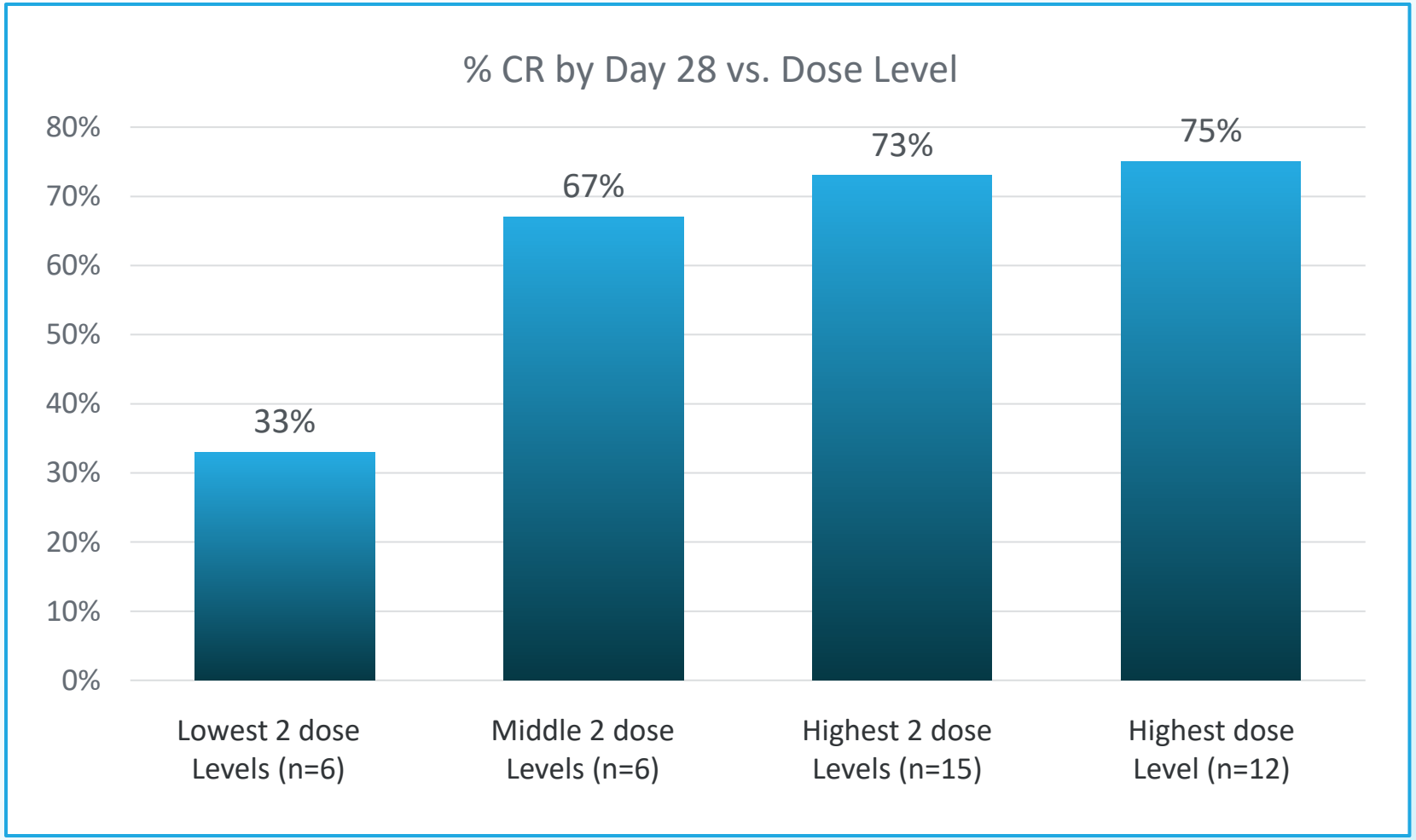
*Interim data published: *J Clin Invest*. (2020) **130**(11):6021-6033

Primary endpoint results from Phase 1/2a Clinical Trial (Day 28)

- 21 evaluable patients
- Disease burden ranged from 5%-98% (median 60%) at enrollment
- 75% of patients achieved CR at highest dose and 73% of CRs were minimal residual disease negative
- No GVHD or neurotoxicity observed
- One-third of patients had only a 50% tissue match, but no differences noted vs. full matches
- 48% of patients that achieved a CR still alive and in CR at 1 year (range 12^{+} months - 31^{+} months)
- Persistence of CARCIK-CD19 measurable up to 21 months in responding patients



Dose-response observed across the dosing range



Dose levels infused:

- N=3 at $1x10^6$ cells/kg
- N=3 at $3 x10^6$ cells/kg
- N=3 at $7.5x10^6$ cells/kg
- N=12 at $15x10^6$ cells/kg

Adverse event data at primary endpoint (Day 28)

#	Age	Dose Level	Day 28				
			Infusion related toxicity	CRS	Neurotoxicity	GVHD	DLT
1	5	1x10^6 cells/kg	No	None	None	None	None
2	27		No	None	None	None	None
3	55		No	None	None	None	None
4	61	3x10^6 cells/kg	No	None	None	None	None
5	44		No	None	None	None	None
6	9		DMSO related transient seizure	None	None	None	None
7	1	7.5x10^6 cells/kg	No	None	None	None	None
8	6		No	None	None	None	None
9	31		No	None	None	None	None
10	39	15x10^6 cells/kg	No	Grade 1	None	None	None
11	62		No	None	None	None	None
12	52		No	Grade 2	None	None	None
13	29		No	Grade 1	None	None	None
14	28		No	None	None	None	None
15	35		No	None	None	None	None
16	60		No	None	None	None	None
17	46		No	Grade 2	None	None	None
18	36		No	None	None	None	None
19	37		No	None	None	None	None
20	38		No	None	None	None	None
21	26		No	None	None	None	None

No SAEs reported to date

CMN-005 compares favorably to FDA approved autologous CAR-Ts

	Yescarta[a]	Kymriah[b]	CMN-005[c]
# Enrolled (treated)	119 (108)	92 (75)	21 (21)
ORR rate	58%	81%	75%
Grade ≥ 3 CRS	11%	46%	0%
Grade ≥ 3 neurotox	32%	13%	0%
Grade ≥ 3 SAEs	52%	73%	0%

[a]Data from ZUMA-1 trial
[b]Data from ELIANA trial
[c]Data from highest dose group (n-12)

CMN-005 has comparable efficacy and superior safety

CMN-005 compares favorably to allo CAR-Ts in development

	Allogene[a]	Precision[b]	CoImmune
Indication	LBCL	B-ALL	B-ALL
Product	Allo-501A	PBCAR0191	CMN-005
N (safety data set)[c]	28	15	21
N (efficacy data set)[d]	6	4	12
ORR rate	33%	75%	75%
CRS (>Grade 3)	11% (0%)	60%(0%)	19% (0%)
Neurotoxicity	21%	20%	0%
Infection	36%	40%	0%
Neutropenia	57%	NR[e]	0%
Grade ≥ 3 SAEs	39%	60%	0%

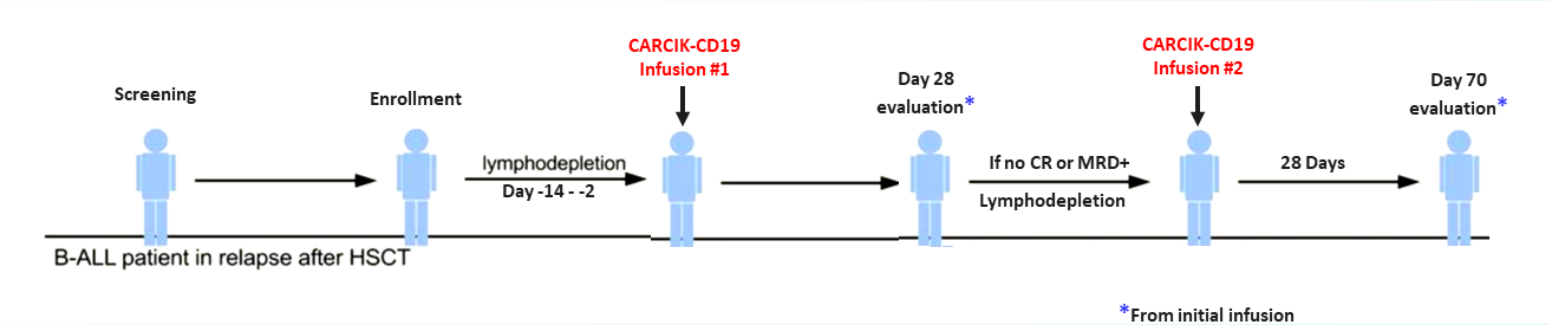
[a]ALPHA-2 trial
[b]ASH December 2021
[c]All patients treated
[d]Patients in highest dose group
[e]Not reported

CMN-005 may have superior efficacy with more favorable safety

On-going Phase 2 ALL Repeat dosing Trial

Title: Measurable residual disease driven strategy for one or two infusions of nonviral, transposon-manipulated CARCIK (CD19) cells. A Phase II study in pediatric and adult patients with relapsed/refractory B cell precursor ALL (BCP-ALL)

- Multicenter, single arm, open label IST trial being conducted in Italy
- Opened for accrual Aug. 2021



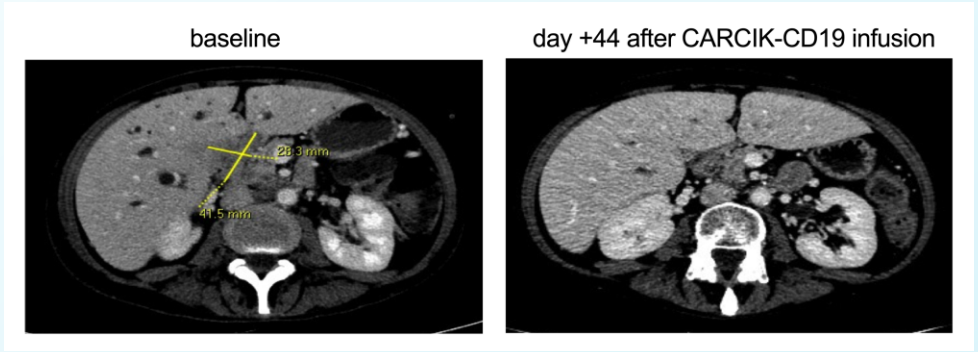
- Co-primary endpoints:
  - ORR at 28 days after (the first) CARCIK-CD19 administration
  - Duration of remission from day 70 for patients who achieved and maintained remission after the first or the second CARCIK-CD19 administration
- Secondary endpoints:
  - Overall survival (i. e. time from infusion to death)
  - Safety of the second administration of allogeneic CARCIK-CD19 cells

As of 4/8/2022: 5 Patients enrolled (4 adults, 1 child), 2 infused so far

Evidence of CAR-CIK effectiveness against solid tumors

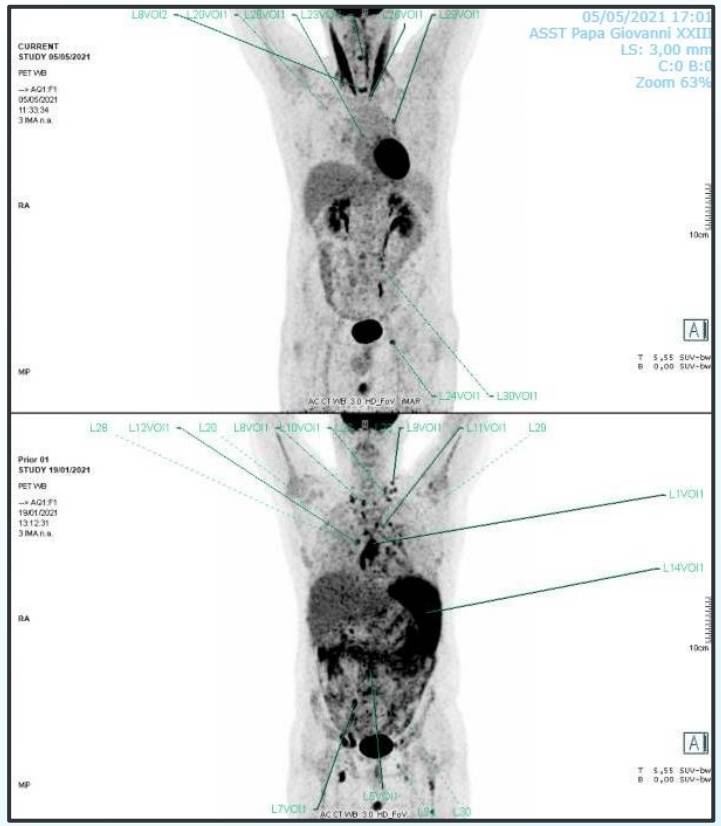
Effective targeting of solid tumor extramedullary disease in 3 patients treated in the Phase 1/2a dose escalation trial

- **Case study #1**: resolved a solid tumor in the liver after CARCIK-CD19 infusion
  - Liver enzymes returned to normal
- **Case study #2**: resolved CNS metastases
- **Case study #3**: Massive blast infiltration of the uterus and annexes with no leukemic blasts in the blood. Completely resolved after CARCIK-CD19 infusion



These cases demonstrate the ability of CAR-CIK cells to extravasate from blood vessels into surrounding tissues to target solid tumors

Mantle cell lymphoma-NHL patient treated with CARCIK-CD19



May 2021

- Substantial resolution of disease after allo CARCIK-CD19 infusion (response on-going)

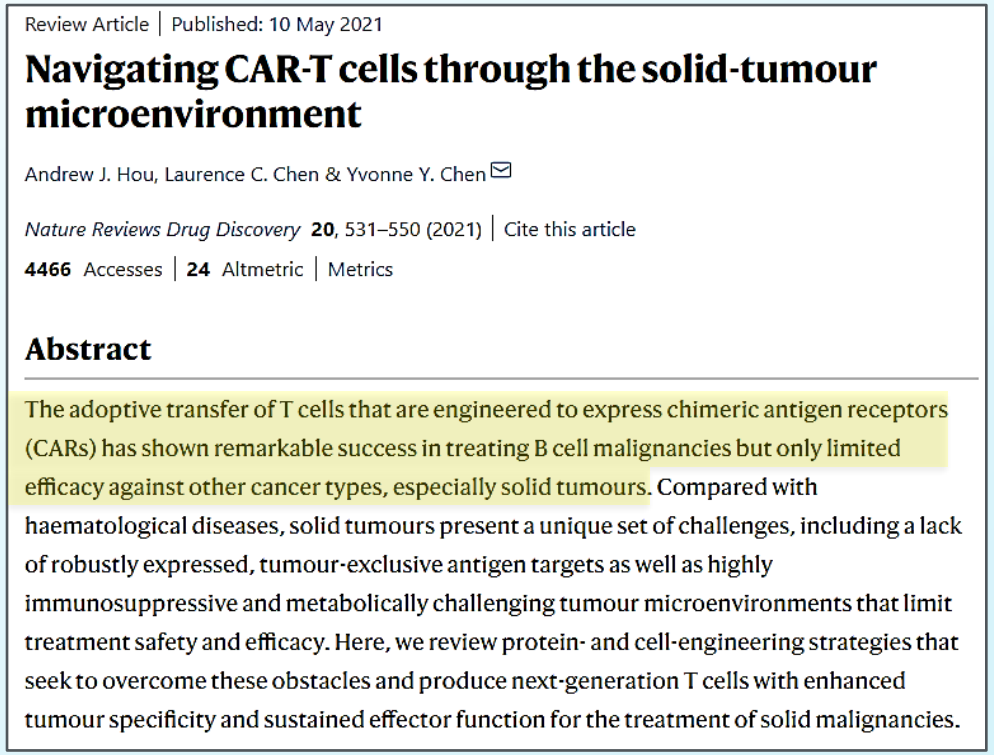
January 2021

- Relapse after all HSCT

Patient treated under compassionate use clinical protocol

Adaptation of CAR-CIK technology for solid tumors

- Solid tumors constitute 95% of the cancer market
- Demonstrated ability of CAR-CIK effectiveness against solid tumors
  - Several patients in the ALL trial developed solid tumors (liver, CNS, Uterus) which resolved after CMN-005 infusion
- CAR-CIK cells may be more effective against solid tumors than CAR-T cells but are likely to require additional technologies in these settings
- CAR-T cells have proven to be ineffective against solid tumors due to the tumor microenvironment and significant safety issues due to off-tumor effects



Review Article | Published: 10 May 2021

Navigating CAR-T cells through the solid-tumour microenvironment

Andrew J. Hou, Laurence C. Chen & Yvonne Y. Chen

Nature Reviews Drug Discovery **20**, 531–550 (2021) | Cite this article

4466 Accesses | **24** Altmetric | Metrics

Abstract

The adoptive transfer of T cells that are engineered to express chimeric antigen receptors (CARs) has shown remarkable success in treating B cell malignancies but only limited efficacy against other cancer types, especially solid tumours. Compared with haematological diseases, solid tumours present a unique set of challenges, including a lack of robustly expressed, tumour-exclusive antigen targets as well as highly immunosuppressive and metabolically challenging tumour microenvironments that limit treatment safety and efficacy. Here, we review protein- and cell-engineering strategies that seek to overcome these obstacles and produce next-generation T cells with enhanced tumour specificity and sustained effector function for the treatment of solid malignancies.

Solid Tumor Challenges to Overcome

- Tumor heterogeneity
- Antigen loss variants
- Target expression on healthy cells
- Tumor microenvironment immune suppression
- Host rejection of CAR-CIK cells

MSK Collaboration: Applying Proprietary MSK Technologies To Accelerate CAR-CIK for Solid Tumors

New Technologies:

- **SEAKER CAR**[1]: Expresses prodrug converting enzyme (e.g., Carboxypeptidase G2 or B-lactamase) to achieve high active anti-tumor drug levels at tumor sites without systemic toxicity
- **Shield CAR**[2]: Expresses the IgG protease ides2 to prevent antibody-based elimination of cells
- **Orexi CAR**[3]: Expresses a secreted form of a high affinity variant of SIRPa to downregulate the 'do not eat me' signal (CD47) on tumor cells to relieve tumor microenvironment immunosuppression
- **IL-18 CAR**[4]: Expresses a secreted form of IL-18 to improve proliferation, persistence and reverse immunosuppression in the tumor microenvironment
- **ADR CAR**[5]: Expresses the allo defense receptor to prevent T/NK cell elimination of cells

Collaboration includes solid tumor target antigen discovery/validation

[1]Nat Chem Biol. (2021) Dec 30 Online ahead of print
[2]Mol Ther. (2021) **29**:10
[3]Unpublished
[4]*Cell Reports* (2018) **23**:2130-2141
[5]*Nature Biotechnology* (2021) **39**:56–63; Non-MSK technology; license not yet secured

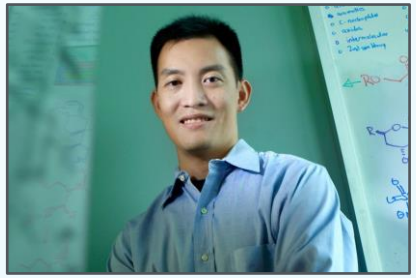
Global leaders from MSK integrating new technologies into CAR-CIK platform

David Scheinberg, MD, PhD

- Chair, Molecular Pharmacology Program, MSK; Director, Experimental Therapeutics Center; Vincent Astor Chair

Renier J. Brentjens, MD, PhD

- Director, Cellular Therapeutics; Associate Chair, Junior Faculty Development, Department of Medicine; Scientific cofounder of Juno

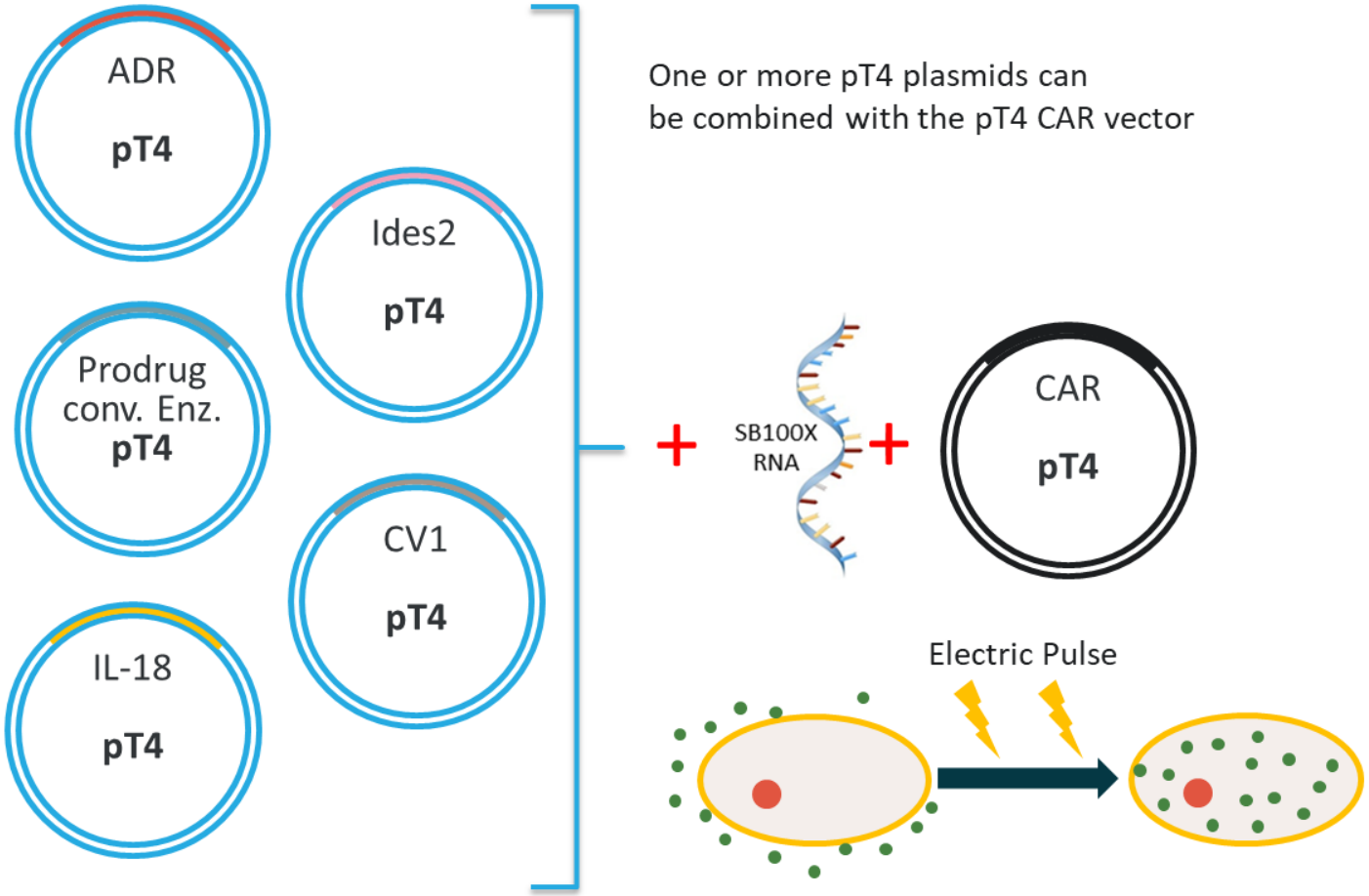


Derek Tan, PhD

- Chair, Chemical Biology Program, MSK
- Director and Professor, Tri-Institutional PhD Program in Chemical Biology

Their laboratories will conduct pre-clinical and clinical trials with the new technologies using CAR-CIK cells

Non-viral gene transfer technology accelerates development



- Each technology requires the addition of another gene in addition to the CAR receptor
- We simply produce pT4 vectors encoding each new gene
- Plasmids can be mixed and matched and co-electroporated to customize functionality to each solid tumor indication

Progress with MSK Technologies

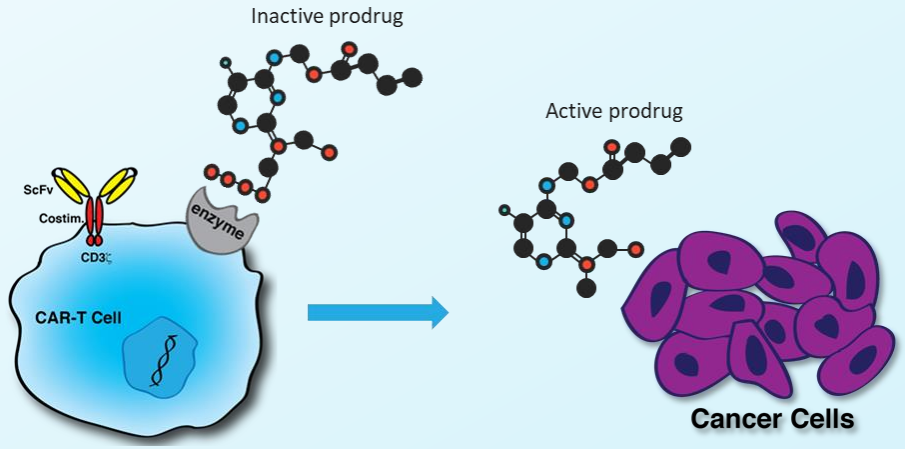
1. SEAKER CAR (MSK)

- What is it?
  - Synthetic Enzyme-Armed Killer Cells
  - Express prodrug converting enzyme (*e.g.*, Carboxypeptidase G2 or B-lactamase)

- How is it used?
  - Administer CAR-CIK-Enzyme followed by inert anticancer prodrug

- What does it do?
  - CAR-CIK cells travel to the tumor site
  - The enzyme converts the prodrug to active drug

- What are the benefits?
  - Creates a high concentration of anti-cancer drug at the tumor sites
  - No active drug detected in the circulation
  - May be required to get CAR-CIK to work in solid tumor indications



See slides 35-36 for *in vitro* proof-of concept

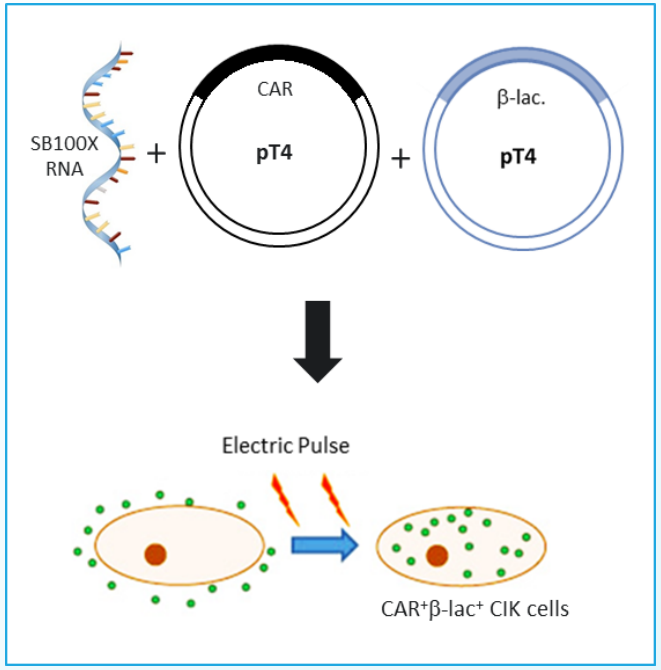
Competition: ADEPT (enzyme conjugated antibody) is closest analogous competitor but is not being pursued due to lack of therapeutic index.

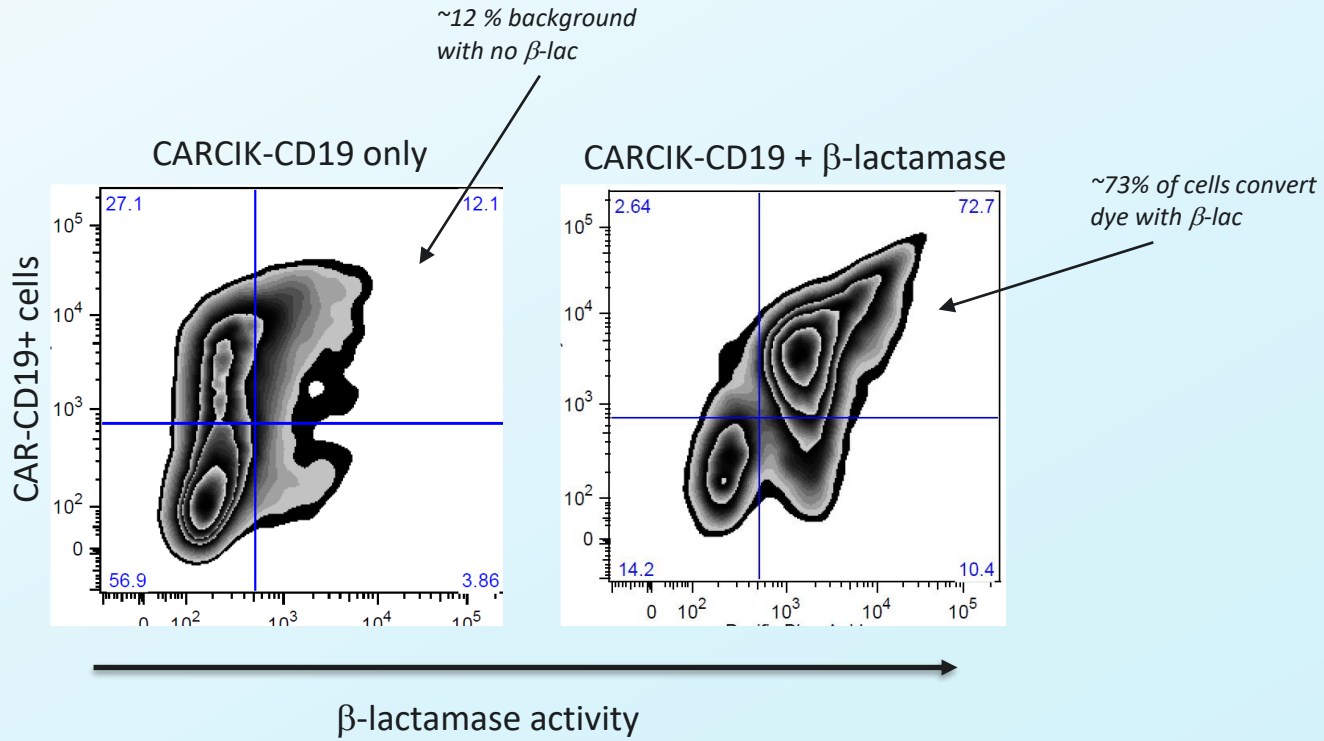
SEAKER CAR (β-lactamase)

In vitro validation of β-lac expression and function

- Cells labeled with a dye that fluoresces green if acted on by β-lactamase
- SEAKER CAR β-lactamase cells maintained CD19 positivity with enzyme activity
  - 73% of the CD3 cells are double positive for CAR and β-lactamase

Test article

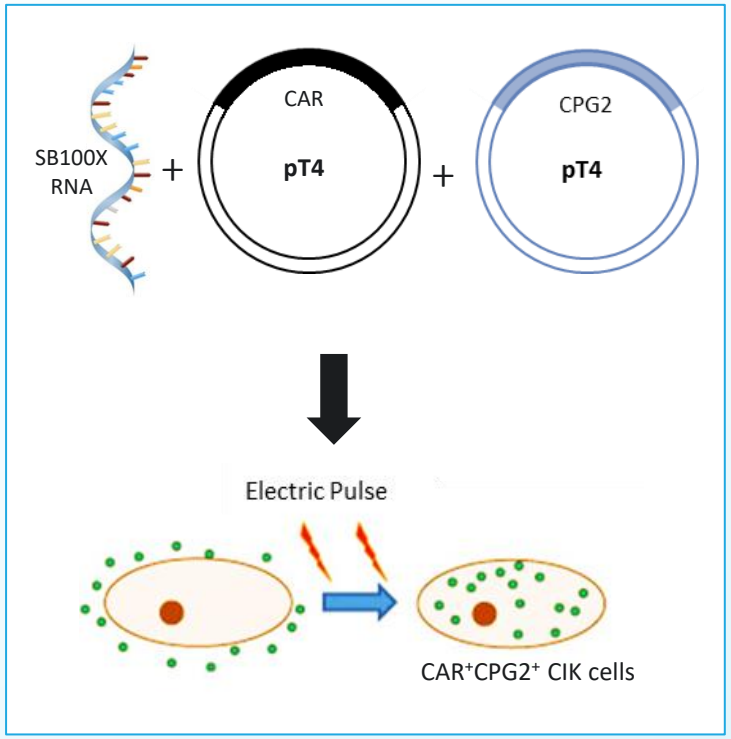




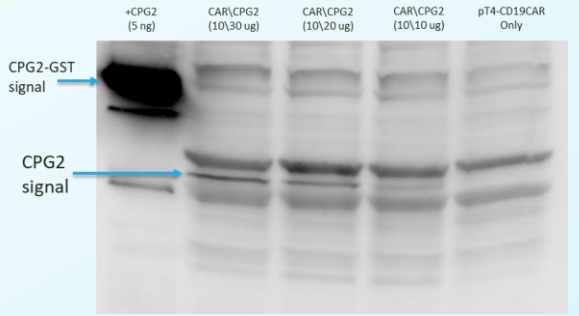
SEAKER CAR (Carboxypeptidase G2)

- SEAKER CAR CPG2 (carboxypeptidase G2)maintained CD19 positivity with enzyme activity
- 64% CARCIK-CD19+ cells

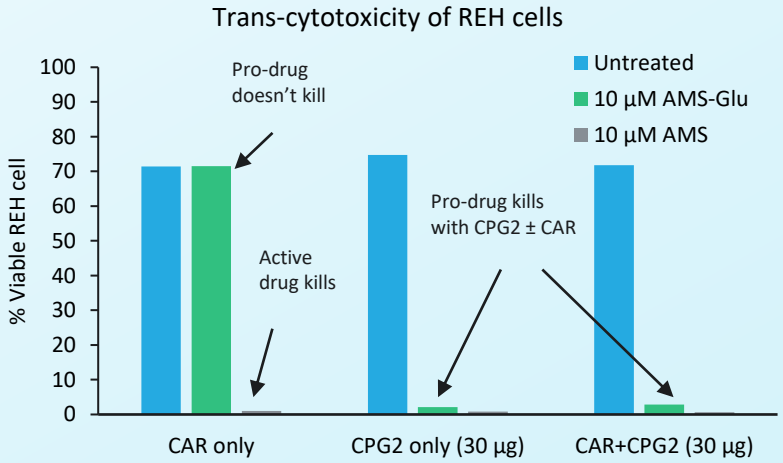
Test article



Western blot detection of CPG2 protein in CIK cells



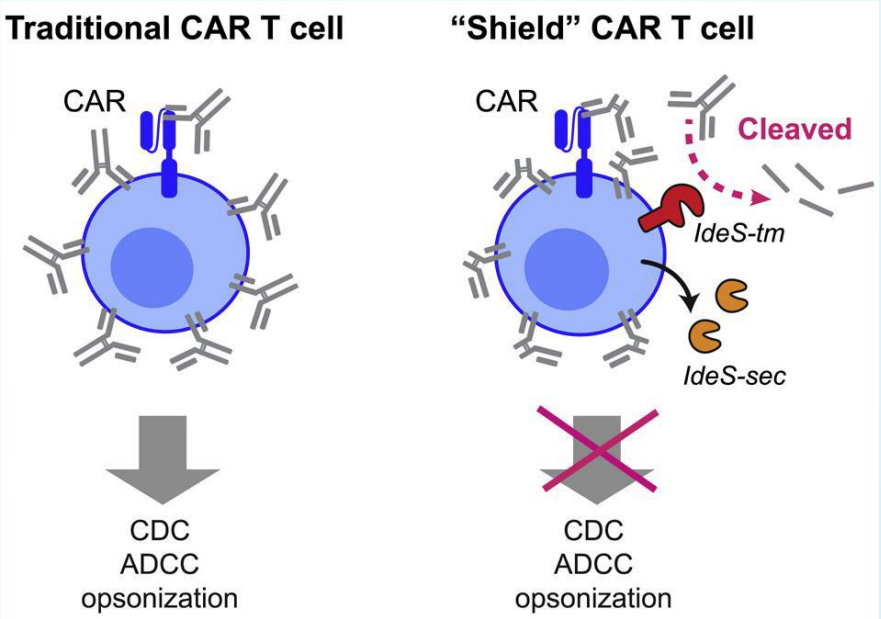
- CARCIK cell Supernatant contains active enzyme



- Only active drug kills without CPG2
- Pro-drug and active drug kill with CPG2

2. SHIELD CAR (MSK)

- What is it?
  - Express the IgG protease Ides2
- How is it used?
  - Administer CAR-CIK-Ides2 as usual
- What does it do?
  - Cleaves antibodies that attack the CAR-CIK cells and coats the cell in harmless Fab fragments
  - Prevents rejection of the allo CAR-CIK cells by antibody attack
- What are the benefits?
  - Increases the persistence of the allo CAR-CIK cells
  - May be necessary for repeat dosing



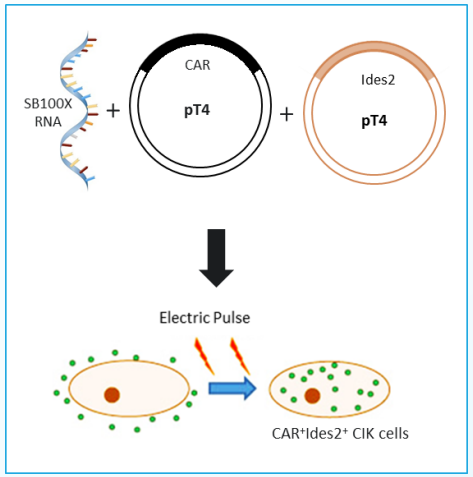
See slide 38 for in vitro proof-of concept

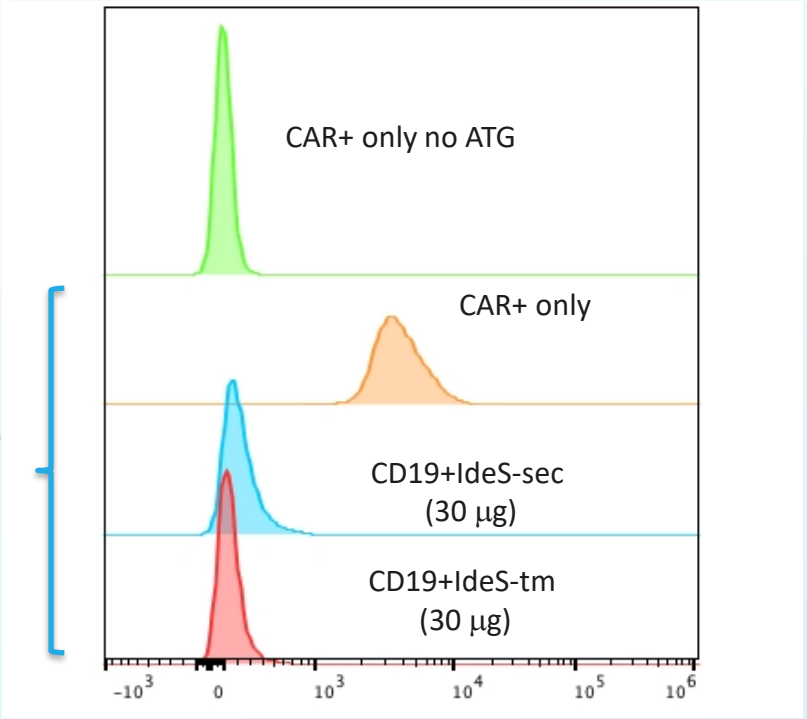
Competition: Nothing that defeats host IgG responses (other than systemic IdeS)

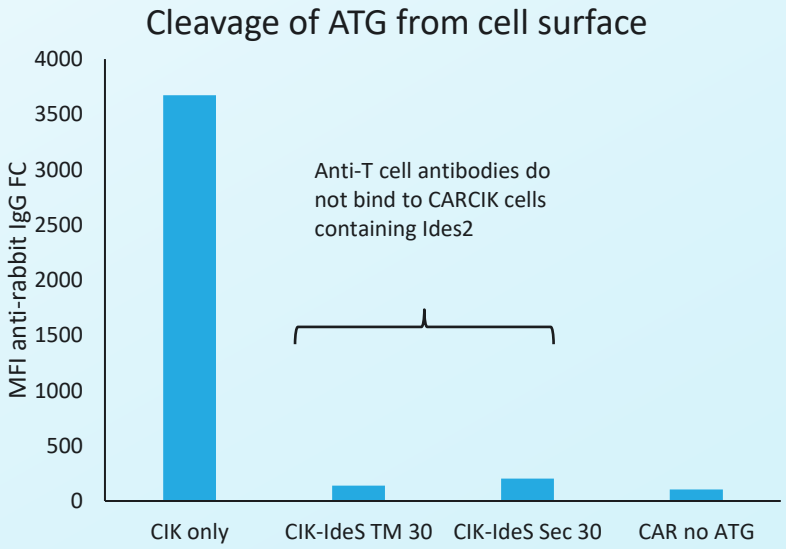
SHIELD CAR

- Both secreted and membrane bound Ides proteins maintain CAR positivity with enzyme activity, 60% (Ides secreted) and 59% (Ides membrane bound)
- IdeS enzymes cleave rabbit anti-thymocyte globulin bound to the surface of CARCIK +IdeS cells
- Both membrane and secreted forms of IdeS are functional

Test article







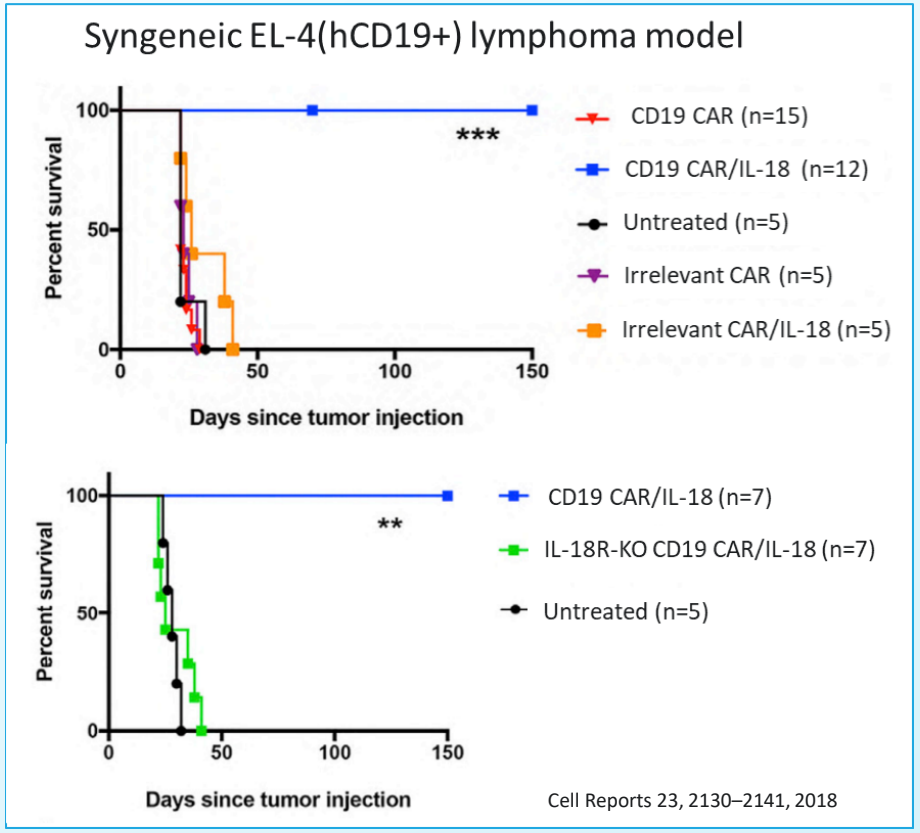
3. Orexi CAR (MSK)

- What is it?
  - Express CV1 protein (secreted form of a high affinity variant of SIRPa)
- How is it used?
  - Administer CAR-CIK-CV1 cells as usual followed by a therapeutic antibody (e.g., Rituxan)
- What does it do?
  - Down regulates CD47 on tumor cells ('do not eat me' signal), activates macrophages, dramatically improves clinical benefit of therapeutic antibodies
- What are the benefits?
  - Provides for added functionality in the tumor microenvironment

Competition: Several companies are in preclinical and early clinical development of molecular CD47 based agents. These agents all suffer from issues with systemic toxicities; large epitope sink; or poor PK.

4. IL-18 CAR (MSK)

- What is it?
  - Express IL-18 cytokine
- How is it used?
  - Administer CAR-CIK-IL18 cells as usual
- What does it do?
  - Delivers IL-18 to the tumor site at high concentration
- What are the benefits?
  - Improves CAR-CIK proliferation and persistence
  - Reverses immunosuppressive tumor microenvironment



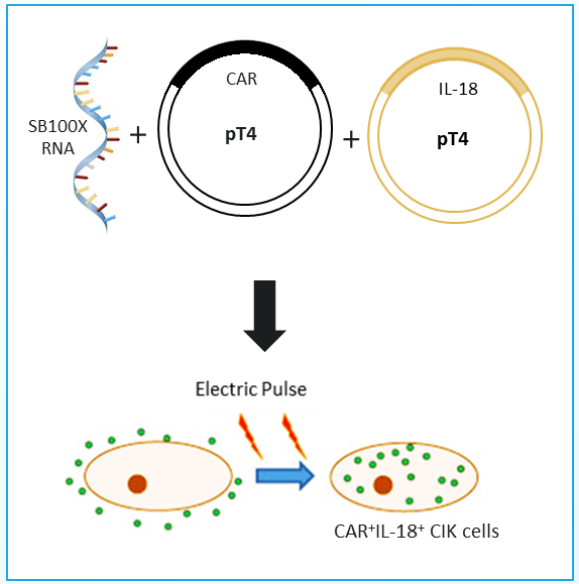
See slide 40 for *in vitro* proof-of concept

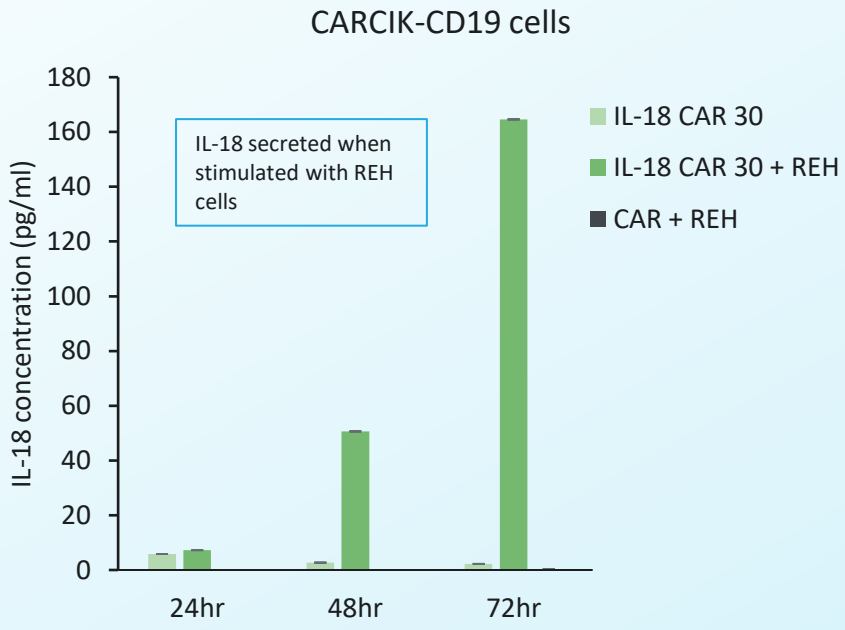
Competition: Many companies are making different armored CARs, but IL18 is patent protected and appears to be more potent that others.

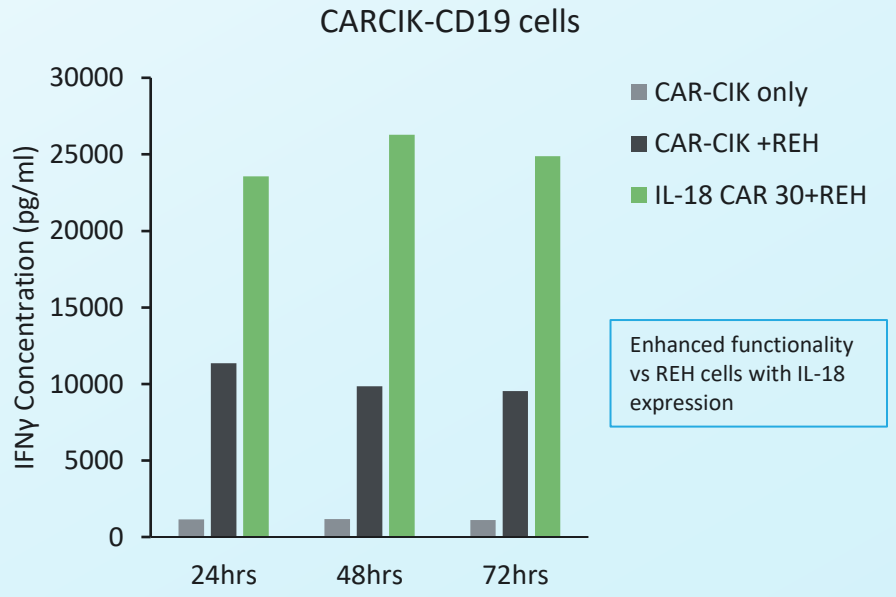
CAR IL-18

- Similar percentage of CAR positive cells in CAR-CIK-CD19 cells and CARCIK-CD19 +IL-18 cells (57% and 46%)
- CARCIK-CD19 cells secreted IL-18 when stimulated with REH (CD19+) cells.
- Enhanced IFN-γ secretion in CARCIK-CD19 +IL-18 cells when stimulated with REH cells versus CARCIK-CD19 only cells

Test article

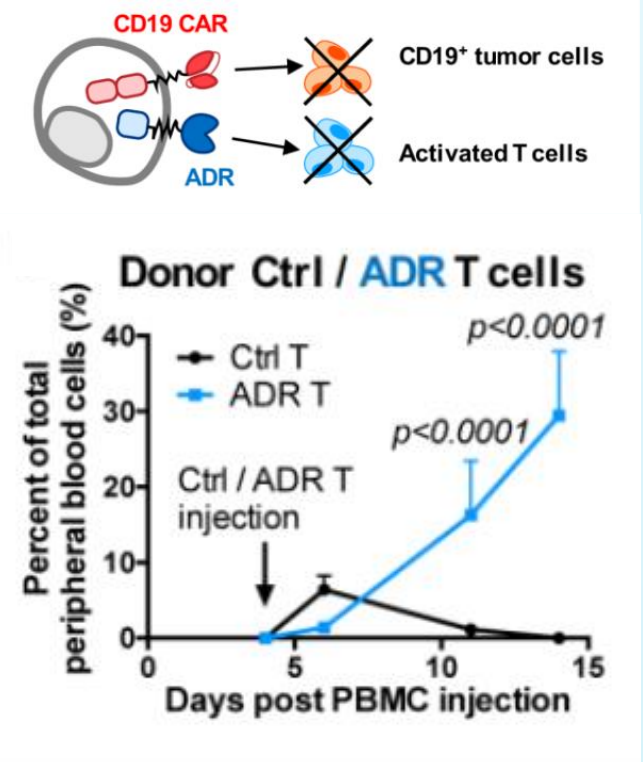






6. ADR CAR

- What is it?
  - Express the AlloImmune Defense Receptor (ADR)
- How is it used?
  - Administer CAR-CIK-ADR as usual
- What does it do?
  - Binds to 4-1BB on activated T cells and NK cells preventing rejection of the CAR-CIK cells
- What are the benefits?
  - Increases the persistence of the allo CAR-CIK cells
  - May be necessary for repeat dosing



Nat Biotechnol. 2021 January ; **39**(1): 56–63

Competition: Nothing that defeats host T/NK cell responses (license not yet secured)

How new technologies address solid tumor challenges

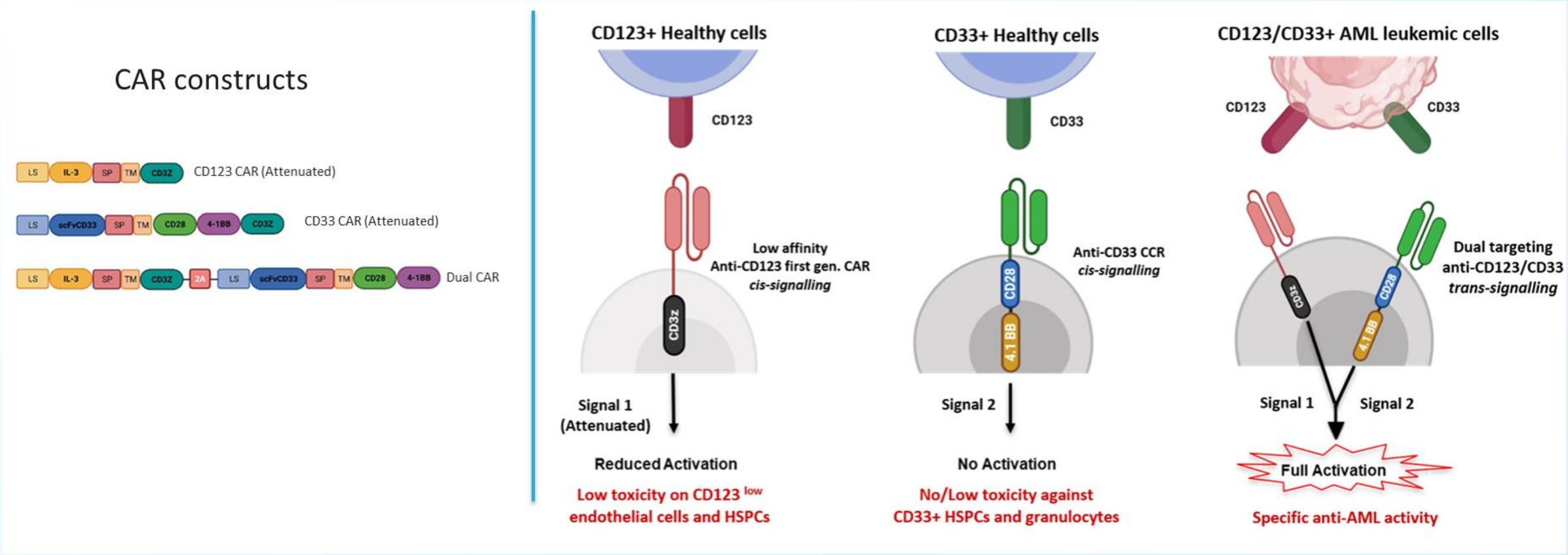
Tumor heterogeneity	Antigen loss variants	Target expression on healthy cells	Tumor microenvironment immune suppression	Host rejection of CAR-CIK cells
SEAKER CAR **CAR-CIK NK activity** **Orexi CAR**	**SEAKER CAR** **CAR-CIK NK activity** **Orexi CAR**	**Bispecific CAR**	**SEAKER CAR** **Orexi CAR** **IL-18 CAR**	**Shield CAR** **IL18 CAR** **ADR**

Strategy for solid tumor CARs

Proof-of-concept with bi-specific CAR for acute myelogenous Leukemia

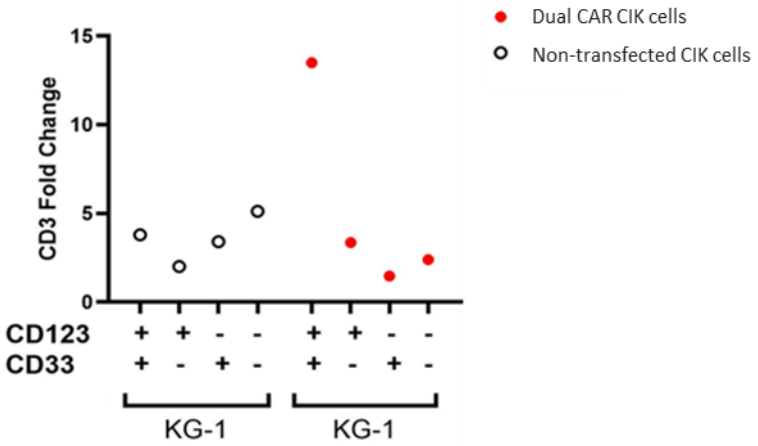
Bi-specific CAR-CIK product for AML developed (CMN-006) [Proof-of-concept for solid tumor CAR strategy]

- Recognition of 2 different tumor antigens required for complete CIK cell activation
- Mitigates risk of healthy cell collateral damage



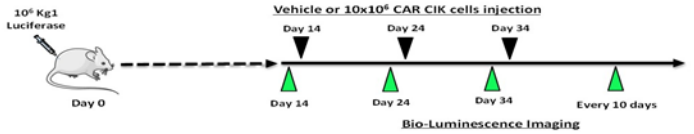
Bi-specific CAR data presented at ASH

Full CIK cell activation requires the presence of both antigens

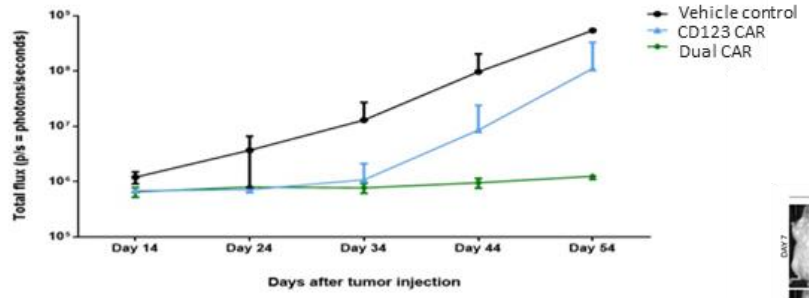


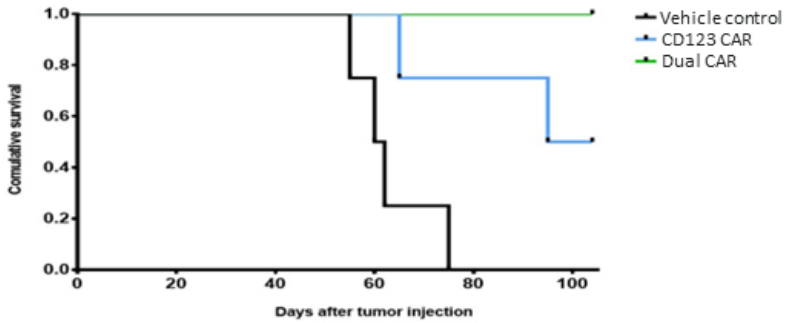
In vitro CIK proliferation after long term co-culture with CRISPR engineered KG1 AML cell line (E:T 1:10)

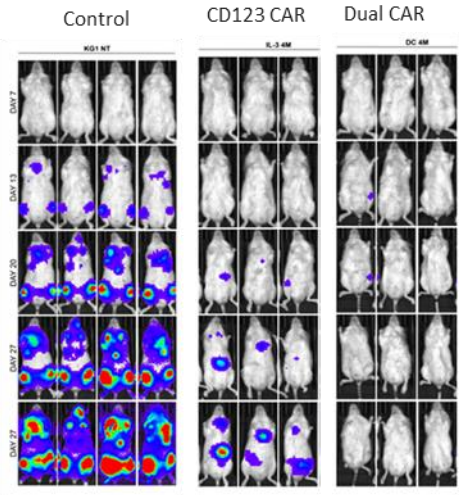
In vivo KG1 AML model: Attenuated CD123 CAR vs Dual CAR



Transacting costimulation confers greater anti-leukemic activity *in vivo* without systemic toxicity







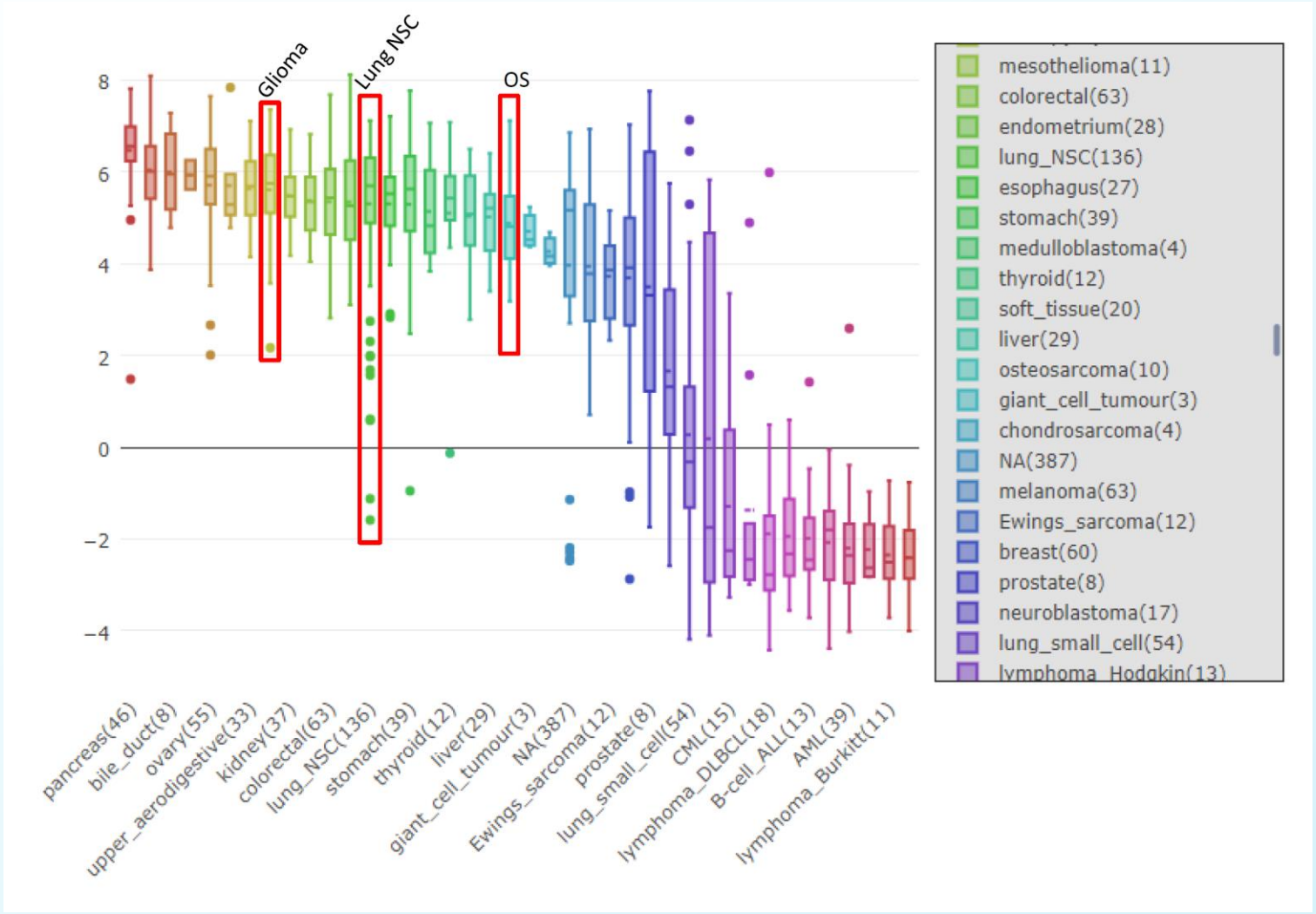
This approach can significantly limit on-target, off-tumor toxicity

MSK Solid Tumor Targets

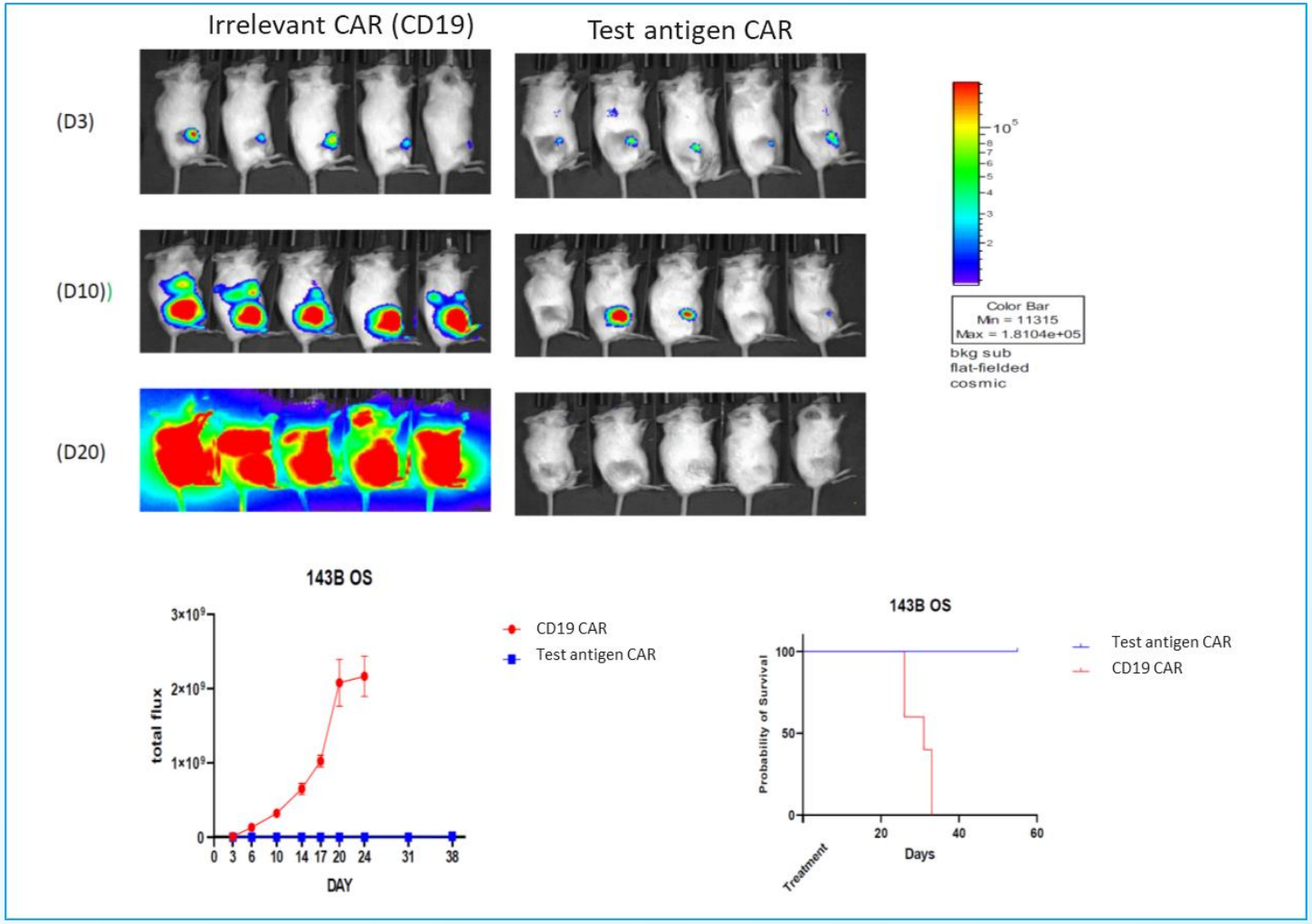
MSK has identified a number of solid tumor target candidates

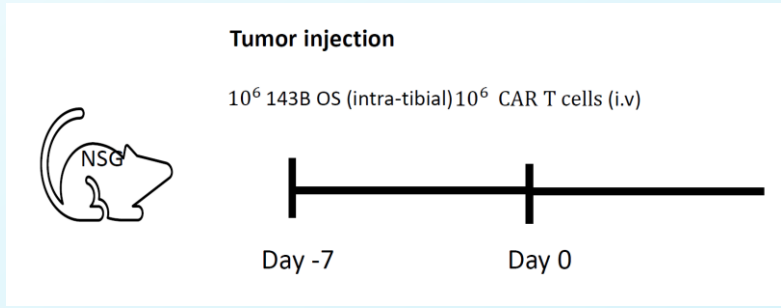
- 6 solid tumor targets being studied
  - Useful for numerous large indications
    - breast, pancreatic, lung, skin, ovarian, colorectal, cervical, bladder, neuroendocrine, cancer-associated stromal fibroblasts – sarcomas, melanomas, glioblastomas

Example of 1 solid tumor target antigen



In vivo activity of solid tumor target antigen CAR T cells in solid tumor xenograft model (orthotopic)





Next generation CAR-CIK technology

Our field is crowded

- There are 778 CAR-T trials in progress worldwide
  - 85% targeting blood cancers
  - 23% targeting solid tumors

- All CAR-T developers are struggling with:
  - Toxicity
  - Only a fraction of the final product is genetically modified (this will be more of a problem not targeting CD19)
  - Manufacturing times are too long (for non-off-the-shelf approaches)
  - Unpredictable *in vivo* expansion

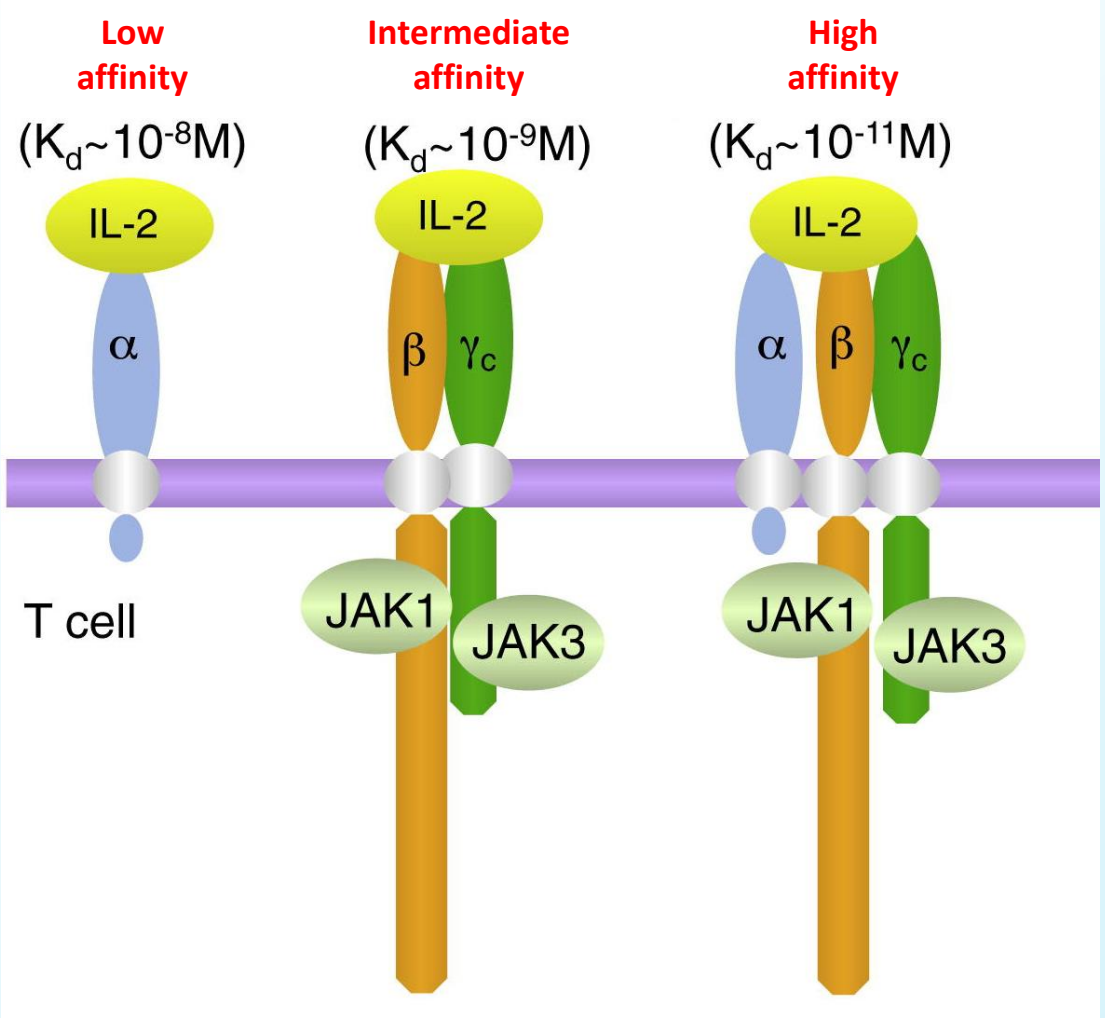
Whoever solves these issues first will dominate the field

Strategy to address challenges with CAR-based therapies

- Use complimentary IL-2 and IL-2R proteins
  - Identified a point mutation in IL-2 that blocks binding to IL-2R
  - Identified a complimentary IL-2R point mutation that restores binding of mutant IL-2

- Designed a bi-cistronic pT4 vector that encodes a CAR and the mutant IL-2R
- Allows the mutated IL-2 to specifically expand only CAR+ cells during manufacturing
- Mutated IL-2 can be administered in vivo to expand CAR-CIK cells without systemic toxicity

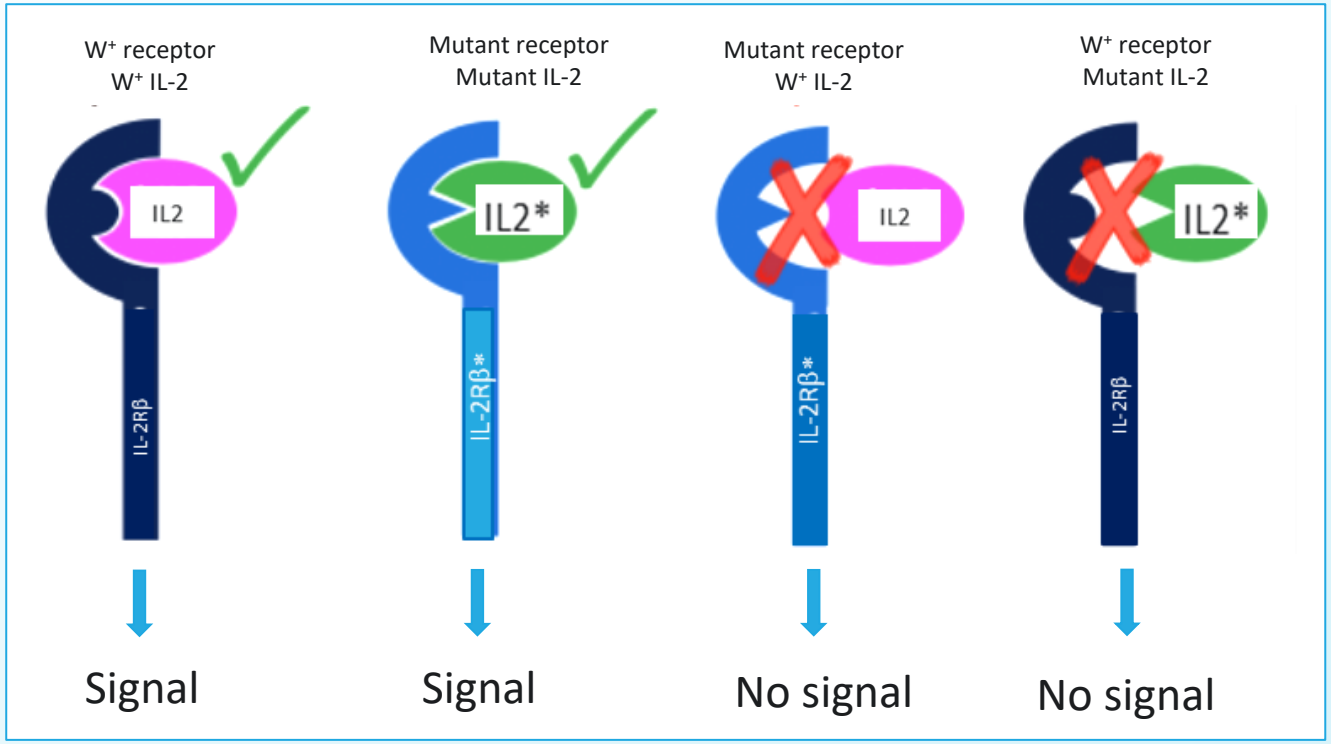
Biology of IL-2/IL-2R (CD25)



Exploiting our growth factor, IL-2

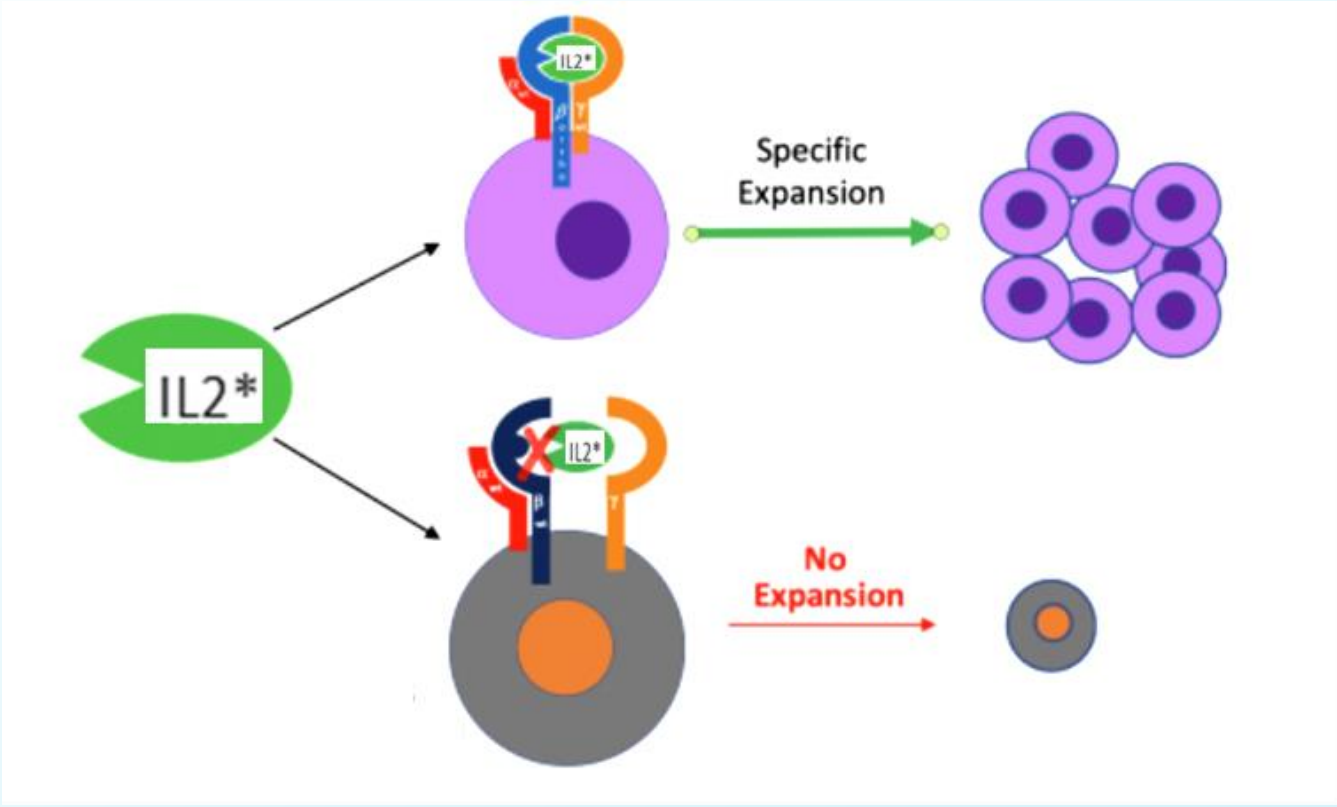
1. Identified hIL-2 point mutation that inhibits activity by 99.8%
   - Binds normally to IL-2Rα but not IL2-Rβ

2. Identified a complimentary point mutation in hIL-2Rβ that restores full activity



CAR-CIK manufacturing with IL-2*/IL-2β*

- Should achieve 100% gene modified cells in final product
- Systemic administration of IL-2* to patients after infusion should expand cells *in vivo* without toxicity
- May allow reducing the effective dose significantly if reliably expanded in vivo
- Would allow shortening of the CAR-CIK manufacturing process (7-14 days?)



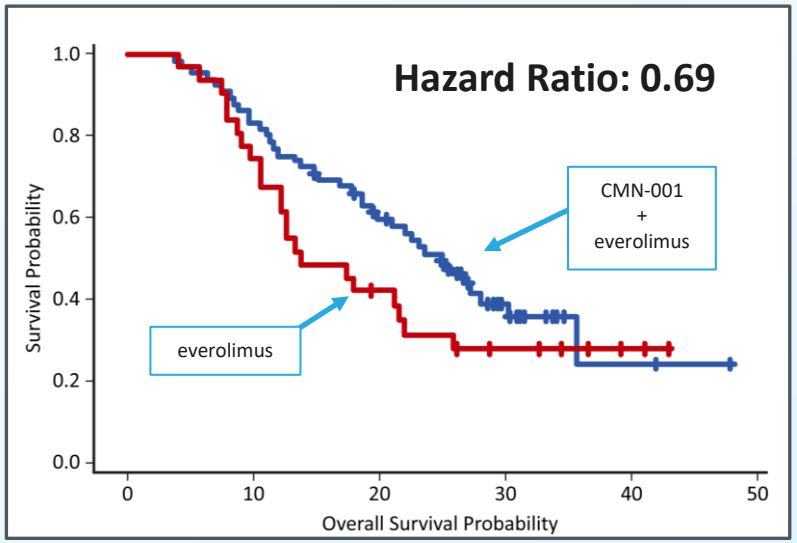
RNA-loaded
Dendritic Cell Platform Technology

CMN-001 synergizes with everolimus

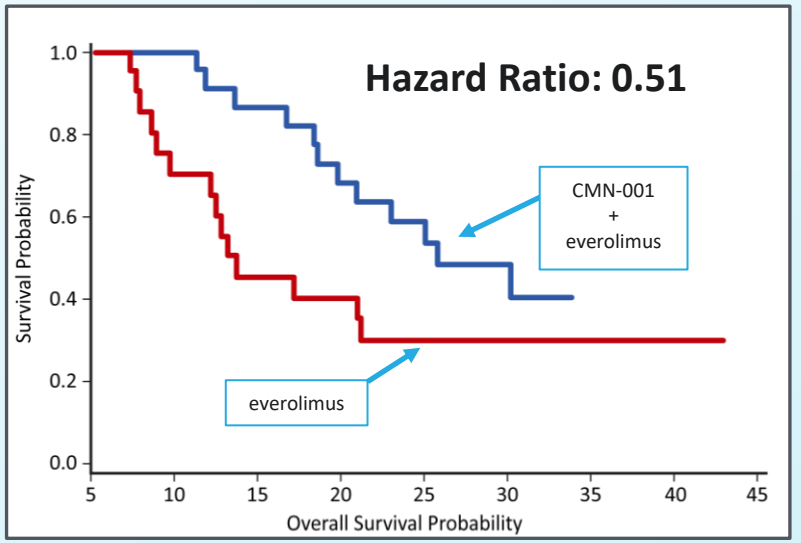
Phase 2b CMN-001-1 trial in advanced RCC

- The Phase 2b trial is designed to reproduce results from a previously conducted randomized trial involving 91 patients showing synergy with mTOR inhibitors
- Previous trial results:
  - For all 91 subjects, CMN-001+SOC (N=60) vs SOC (N=31) , HR=0.69
  - For subjects treated similar to Phase 2b trial design, CMN-001+SOC (N=22) vs SOC (N=20) , HR=0.51

All 91 patients



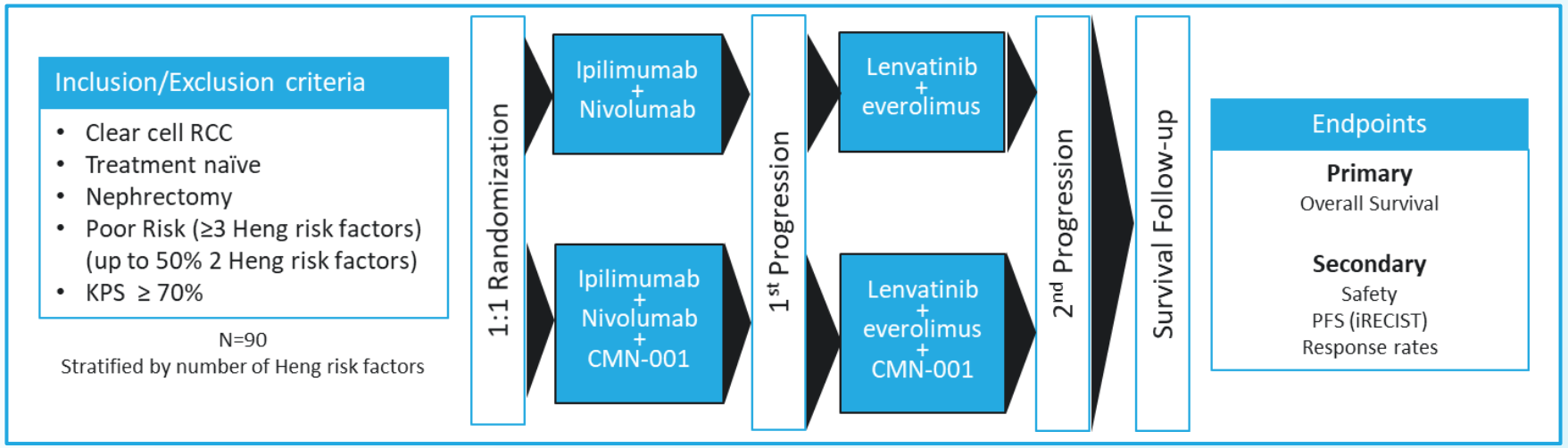
42 patients receiving mTOR *after* CMN-001
(Phase 2b trial design)



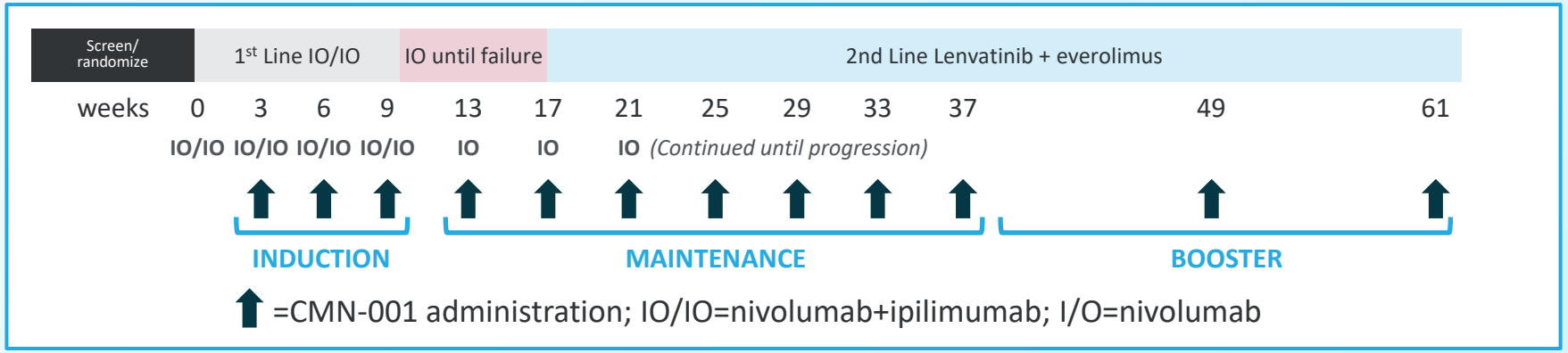
CoImmune scientists discovered the molecular basis of the synergy between CMN-001 and mTOR inhibitors – Patent filed

CMN-001-1 Phase 2b Trial Design

Overview



Detail



Targeting areas of significant unmet needs in rapidly growing immuno-oncology market

Immuno-oncology therapies market

- Approximately $14 billion in 2019 and estimated to reach $34 billion by 2024 (Drug Development & Delivery)

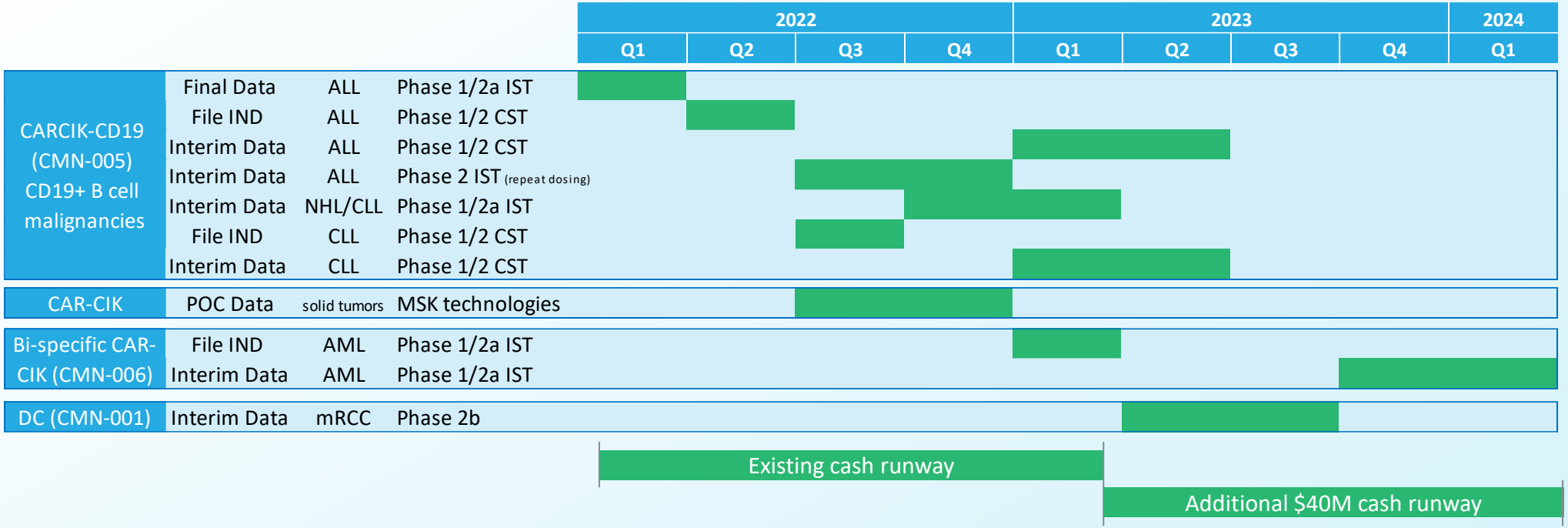
CAR-T market

- $611 million in 2019 and estimated to reach $3.2 billion in 2023 at a compounded annual growth rate (CAGR) of 51.1% (Research & Market)

Kidney cancer market

- Estimated to reach $6.3 billion by 2022 at a CAGR of 5.4% (Grand View Research)

Use of $40M in Proceeds/Upcoming Milestones



ALL = Acute Lymphoblastic Leukemia; NHL = Non-Hodgkin's Lymphoma; CLL = Chronic Lymphocytic Leukemia; AML = Acute Myeloid Leukemia; DC = RNA-loaded Dendritic Cells; mRCC = Metastatic Renal Cell Carcinoma; MSK = Memorial Sloan Kettering Cancer Center; IST = Investigator sponsored trial; CST = Corporate sponsored trial; POC = Proof of concept

Intellectual Property related to CAR-CIK

- Sleeping Beauty 100X transposon and transposase compositions and methods
  - Exclusively licensed from Max Delbruck Center in the field of CAR-CIK
  - 2 U.S. patents and 2 U.S. pending patent applications, 6 foreign patents and 6 pending foreign patent applications
  - Expected Expiration: 2028 to 2037

- Combinations of CAR-CIK with inotuzumab ozogamicin
  - Co-Owned with Fondazione Fondazione M. Tettamanti (with exclusive license)
  - 1 pending U.S. patent application and 5 pending foreign patent applications
  - Expected Expiration: 2040

- Combinations of CAR-CIK with MSK technologies
  - SEAKER: 1 pending U.S. patent application, 3 pending foreign applications; 2039 expiration
  - Shield (ides2): 1 pending PCT International patent application; 2040 expiration
  - Orexi (CV1): 1 pending PCT International patent application; 2038 expiration
  - IL-18: 1 pending U.S. patent application and 3 pending foreign applications; 2037 expiration

Intellectual Property related to CMN-001

- Compositions of Matter and Manufacturing Methods
  - 6 U.S. patents, 1 U.S. patent application and 37 foreign patents
  - Expected Expiration: 2025-2029 in the US and 2025-2027 in the rest of the world

- Automation Equipment that could be implemented to manufacture CMN-001
  - 8 U.S. patents, 9 foreign patents and 2 foreign patent application
  - Expected Patent Expiration: 2027-2033
  - Trade Secret protection of cellular automation equipment does not expire

- Combinations of CMN-001 with mTOR inhibitors
  - 1 pending PCT International patent application
  - Expected Expiration: 2041