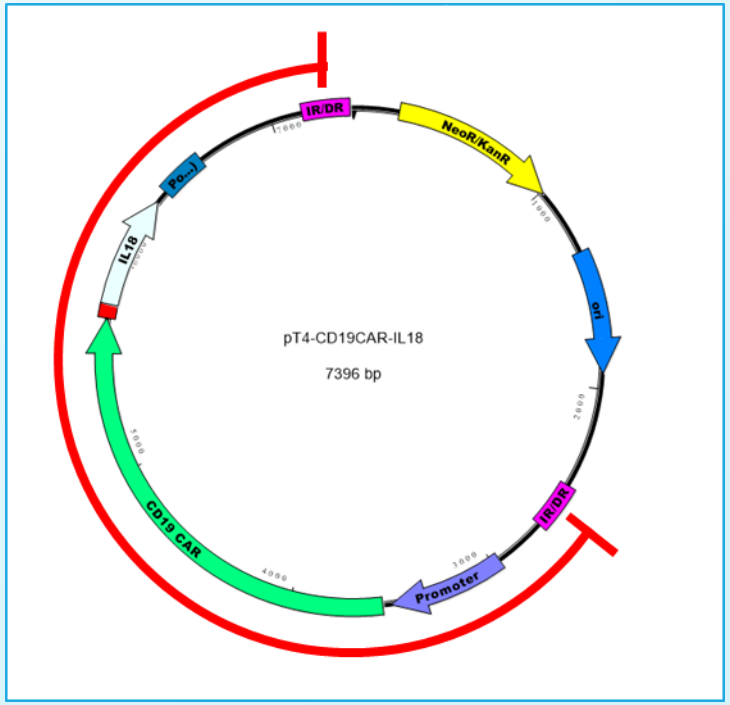
Armored CARCIK-CD19 for B cell malignancies

CMN-008 (Armored CAR-CIK cells)

- Technology acquired from Memorial Sloan Kettering
  - CIK cells genetically modified using SB100X mRNA + pT4 vector encoding both CD19 CAR and IL-18
  - Referred to as ‘armored CAR’

- Constructed a bicistronic vector encoding both CAR-CD19 and IL-18
  - The transposon inserted into the chromosome contains both genes (shown in red)
  - Ensures that all CAR^{+} cells are IL-18^{+}



Market concerns in B-cell malignancy

Limitations of CAR-T therapeutics in hematologic malignancies

The following based on 16 U.S. FACT* accredited cell therapy sites surveyed in 2022 on their plans for using CD19 CAR-T to treat B cell malignancies

- Lower than expected usage
  - Primarily due to reimbursement issues and poor community center referrals
  - Of 16 FACT accredited sites surveyed, approximately 2500 patients treated annually of which ~30% receive a cell therapy, 75% of which are commercial and 25% pre-commercial

Cost and patient access

- CAR-T growth to be driven by outpatient usage
  - Expertise in managing side effects to allow some outpatient use
  - High risk patients can be identified for inpatient treatment

Safety

- Strong preference for reduced vein-to-vein time
  - Currently 3-4 weeks for approved therapies
  - ~50% of patients require bridging therapy resulting in ~7% with AEs that delay or prevent CAR-T administration
  - Opportunity for allo therapies, especially off-the-shelf products

Product availability

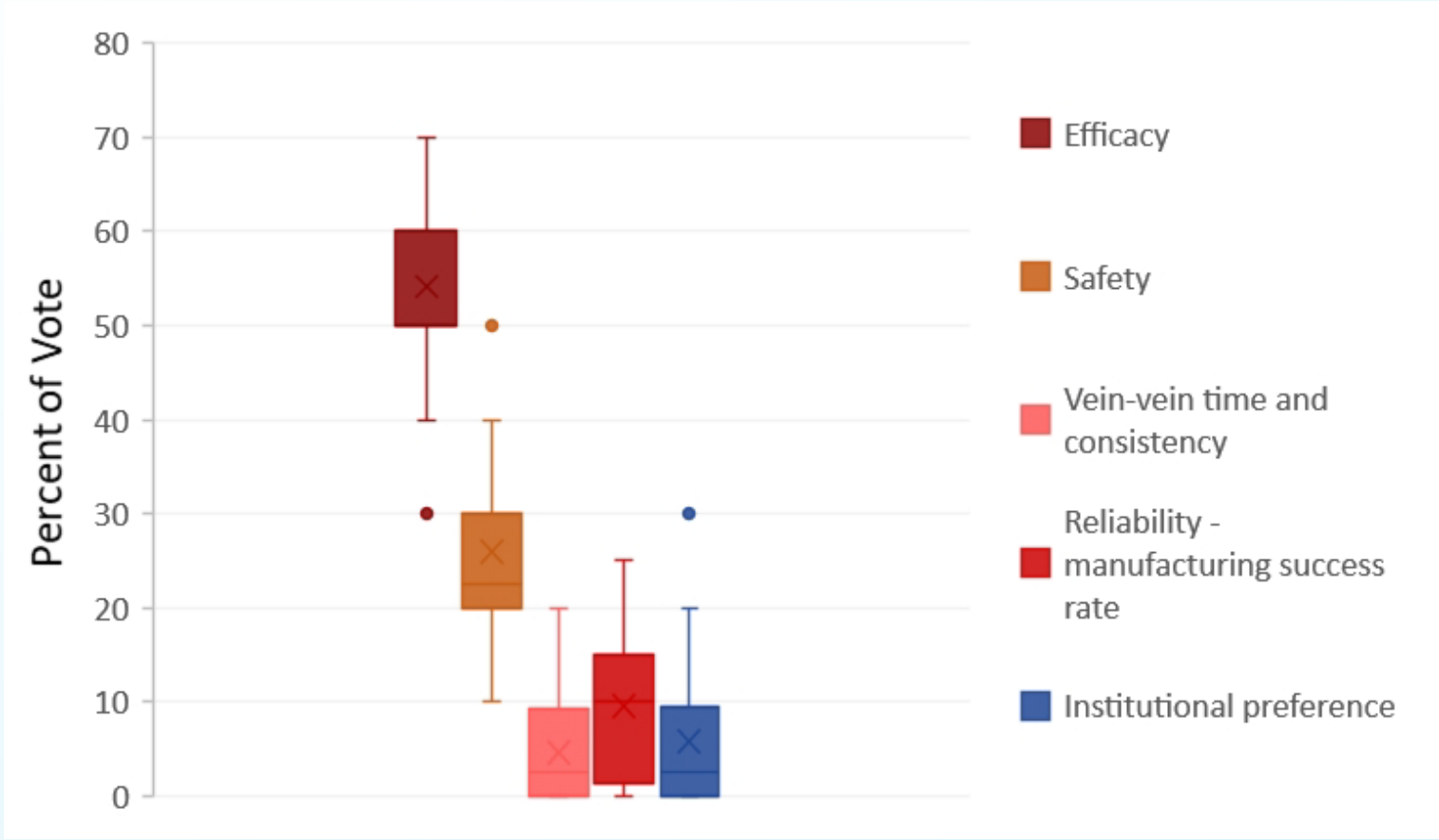
**FACT is an internationally recognized accrediting body for hospitals and medical institutions offering cell therapies*

How do PIs decide which CAR-T therapy to give their patients?

Efficacy includes CR rate, MRD negativity and durability of response

Low premium on safety reflects confidence in managing adverse events

Relative importance of CAR-T attributes in choosing a CAR-T therapy



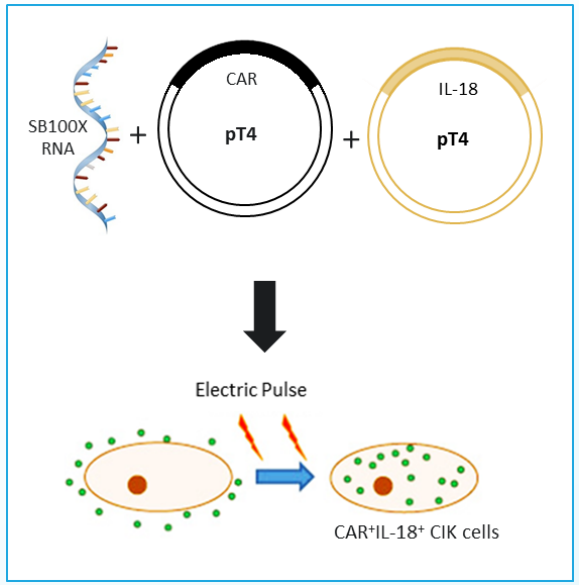
Source: Wells Fargo Research. Whiskers denote the range, solid area first and third quartile above the median (line),X the mean and dots outlier values.

CMN-008 addresses the market concerns

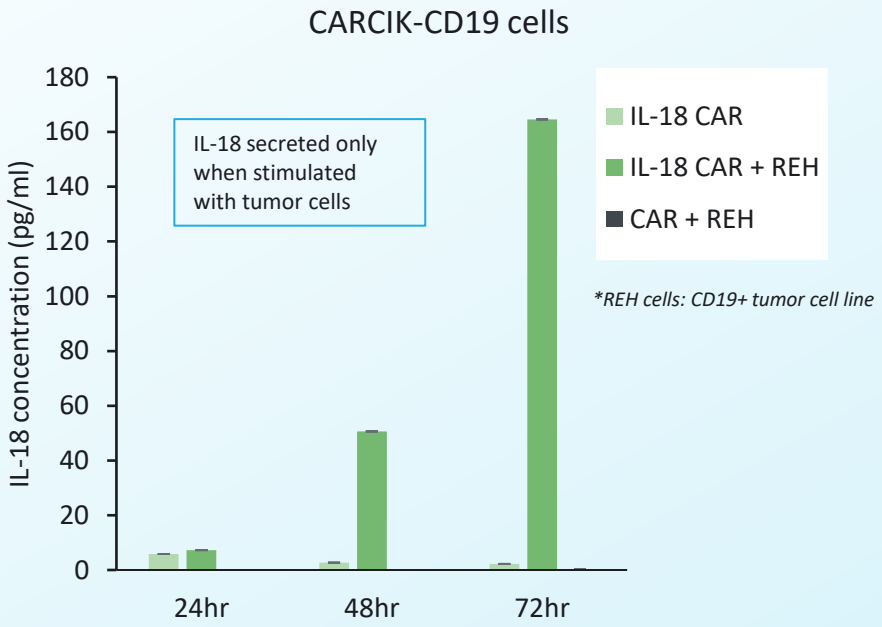
- Safety
  - IL-18 only secreted in the presence of $CD19^{+}$ cells (no systemic toxicity observed)
  - Does not require lymphodepletion in animal models (game changer if same true for patients)
  - Suitable for outpatient usage and administration at community sites (allo product avoids complex autologous logistics)
  - Lower dose required for same efficacy in animal models
- Efficacy
  - Increased anti-tumor activity
  - Increased *in vivo* expansion (unaffected by homeostatic cytokines)
  - Enhanced persistence and durability of responses (deeper and longer lasting B cell aplasia in animal models)
  - Recruits other types of immune cells for a more complete anti-tumor response (CD8+ , NK, NKT, dendritic cells)
- Reduced lead time
  - Requires only a 17-day process (current autologous therapies have 3-4 week lead time)
- Affordability will ease reimbursement issues
  - Streamlined manufacturing process and replacing retrovirus with Sleeping Beauty 100X greatly reduces COGS

Armored CAR technology works with CIK cells

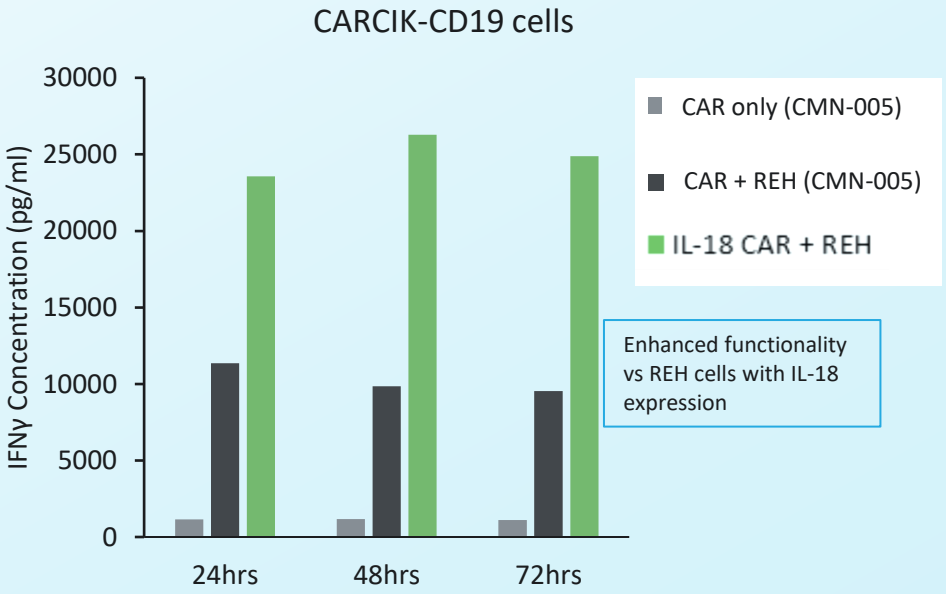
Test article



Built-in safety – No IL-18 secretion without tumor cells present

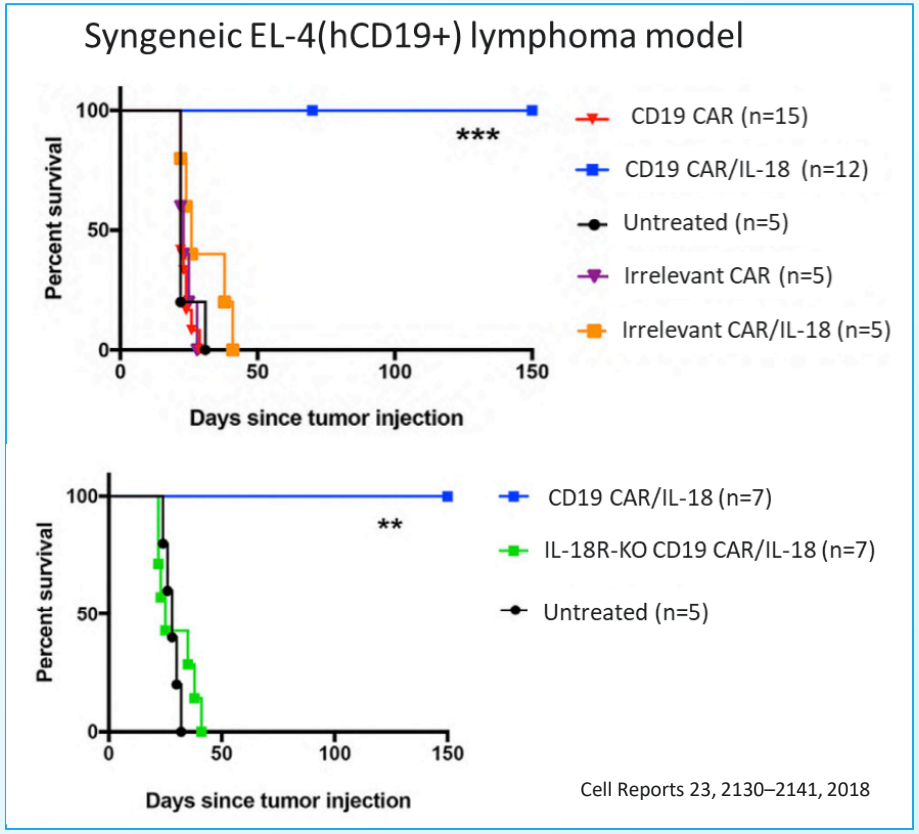


CMN-008 more than doubles the anti-tumor activity of CMN-005



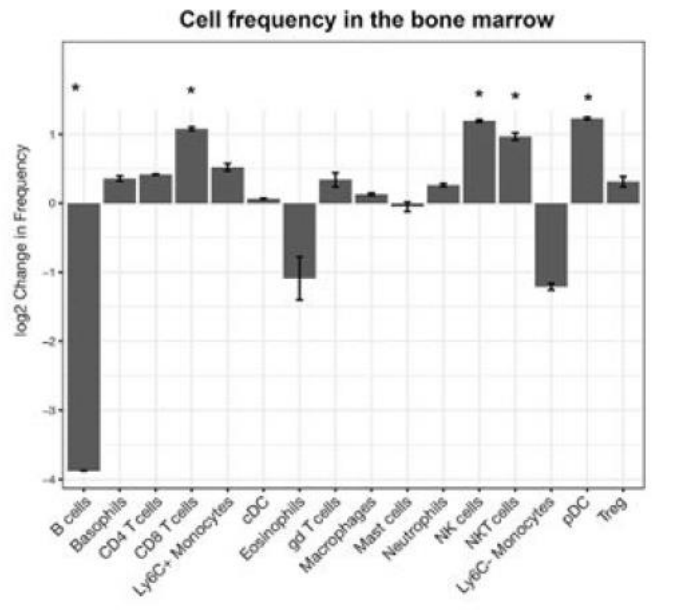
Published data: IL-18 CAR-T cells fully effective even without lymphodepletion

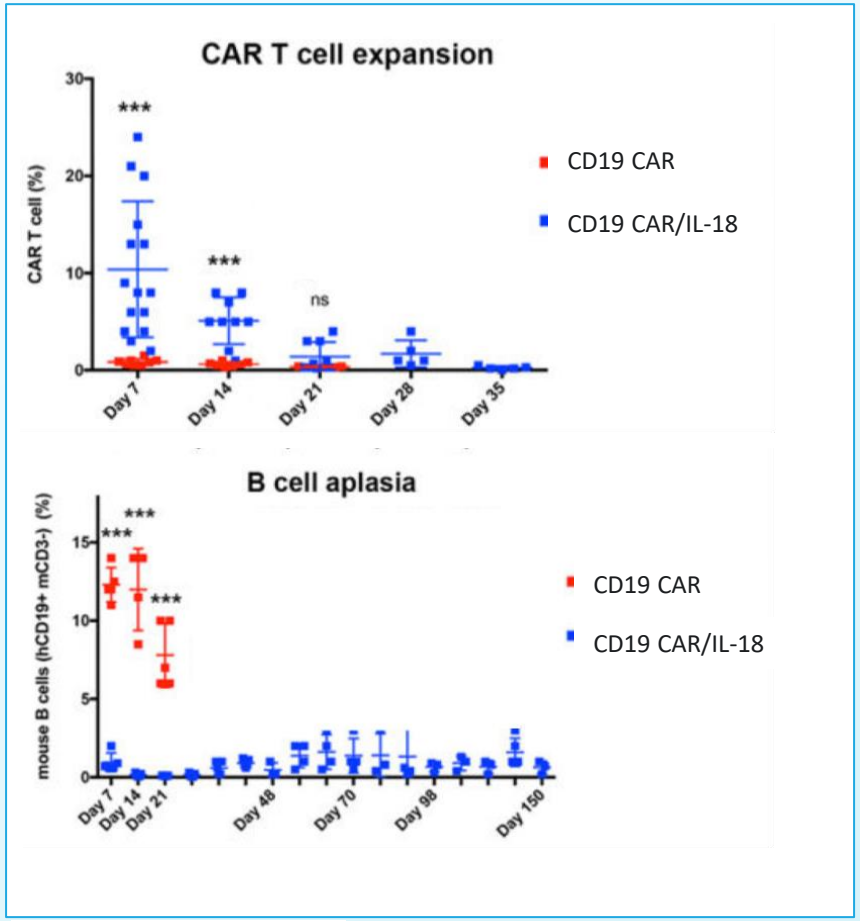
- Standard CAR-T cells are not effective without lymphodepletion
- Armored CAR-T cells are highly effective even without lymphodepletion (Top)
- IL-18 is responsible for the enhanced activity since armored CAR-T cells are ineffective in IL-18 receptor knockout mice (Bottom)



Published data: IL-18 CAR-T have improved properties

- Armored CAR-T cells expand rapidly *in vivo* (Top right)
- Armored CAR-T cells induce deeper and durable B cell aplasia *i.e.*, anti-leukemia effect (Bottom right)
- Armored CAR-T cells recruit other immune cells to the bone marrow (Below)





Cell Reports 23, 2130–2141, 2018

Clinical development plan

cōIMMUNE

CMN-008 clinical development plan

- Maintain support for clinical trials with CMN-005 in Italy to keep clinical data flowing
  - Repeat dosing study in ALL
  - NHL/CLL study: Inclusion/exclusion criteria targets patients ineligible for approved or about to be approved therapies

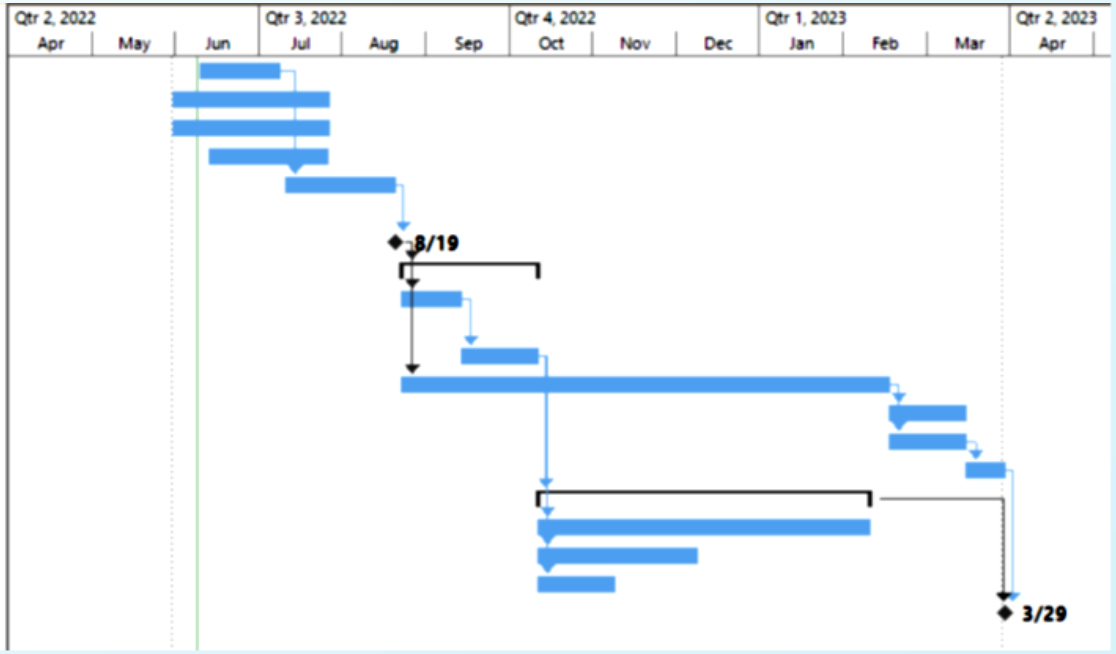
- Launch CoImmune's corporate trial with CMN-008
  - Will incur a delay in starting the trial (but will produce data prior to next financing)
  - Will need to start with Phase 1 (but Phase 2 could be for registration)
  - If positive phase 1 data, we will seek RMAT designation (includes fast track and breakthrough therapy designation)

Benefits of using CMN-008 as CoImmune's first-in-man trial

- Expectation of increased CR rate and durability without significant safety issues
- Distinguishes CoImmune further from competitors – World's first armored CAR-CIK trial
  - Some validation from Carl June at U. Penn: Started a Phase 1 trial in May 2021 with autologous virus-modified IL-18/CAR-T cells using reduced fixed dose without preconditioning lymphodepletion in CLL/NHL patients
- Demonstrates earlier than expected adoption of MSK technology, highlighting the value of the collaboration
- Provides human safety data for deploying armored CAR technology in solid tumors

IND Submission planned by end of Q1 2023

Task Name	Duration	Start	Finish	Predecessors
Vector Construction in Mol Bio R&D grade	20 days	Fri 6/10/22 8:00 AM	Fri 7/8/22 5:00 PM	
Product Characterization w/ 2-Plasmid Workflow	40 days	Tue 5/31/22 8:00 AM	Tue 7/26/22 5:00 PM	
New Assay Development for IL-18 and new CQA (CD56)	40 days	Tue 5/31/22 8:00 AM	Tue 7/26/22 5:00 PM	
Synthetic Vector Production by GeneArt (4 Constructs)	30 days	Mon 6/13/22 8:00 AM	Mon 7/25/22 5:00 PM	
4 Vector Evaluation in Immunology (at least 2 Donors, plasmid titration)	30 days	Mon 7/11/22 8:00 AM	Fri 8/19/22 5:00 PM	1
Selection of Final Vector	0 days	Fri 8/19/22 5:00 PM	Fri 8/19/22 5:00 PM	5
Development Runs with Research Grade Plasmid	**35 days**	**Mon 8/22/22 8:00 AM**	**Mon 10/10/22 5:00 PM**	**6**
Production for Assay Development/Qualification, CQA Confirmation	15 days	Mon 8/22/22 8:00 AM	Mon 9/12/22 5:00 PM	6
Production for IND Enabling Studies	20 days	Tue 9/13/22 8:00 AM	Mon 10/10/22 5:00 PM	8
GMP Plasmid Production by VGXI	120 days	Mon 8/22/22 8:00 AM	Wed 2/15/23 5:00 PM	6
Plasmid Comparability Study	20 days	Thu 2/16/23 8:00 AM	Wed 3/15/23 5:00 PM	10
GMP Runs w/ GMP Plasmid	20 days	Thu 2/16/23 8:00 AM	Wed 3/15/23 5:00 PM	10
QC Studies w/ GMP lots (In-Use Stability, Compatibility)	10 days	Thu 3/16/23 8:00 AM	Wed 3/29/23 5:00 PM	12
IND Enabling Studies	**80 days**	**Tue 10/11/22 8:00 AM**	**Wed 2/8/23 5:00 PM**	**9**
Animal Studies	80 days	Tue 10/11/22 8:00 AM	Wed 2/8/23 5:00 PM	9
Integration Analysis	40 days	Tue 10/11/22 8:00 AM	Wed 12/7/22 5:00 PM	9
TCR-Vb Analysis	20 days	Tue 10/11/22 8:00 AM	Mon 11/7/22 5:00 PM	9
IND Submission	0 days	Wed 3/29/23 5:00 PM	Wed 3/29/23 5:00 PM	14,13



Milestones through 2024

Revised Milestone Chart

				2022				2023				2024			
				Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
CARCIK-CD19 (CMN-005) CD19+	Final Data	ALL	Phase 1/2a IST												
	Interim Data	ALL	Phase 2 IST (repeat dosing)												
	Interim Data	NHL/CLL	Phase 1/2a IST												
CARCIK-CD19 (CMN-008)	File IND	ALL	Phase 1 CST												
	Interim Data	ALL	Phase 1 CST												
CAR-CIK	POC Data	solid tumors	MSK technologies												
Bi-specific CAR-CIK (CMN-006)	File IND	AML	Phase 1/2a IST												
	Interim Data	AML	Phase 1/2a IST												
	File IND	AML	Phase 1/2a CST												
	Interim Data	AML	Phase 1/2a CST												
DC (CMN-001)	Interim Data	mRCC	Phase 2b												

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