



TAKEDA ONCOLOGY: INNOVATIVE CELL THERAPIES & NEW FRONTIERS IN IMMUNO-ONCOLOGY



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 Tokyo
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Better Health, Brighter Future


A CURATIVE-INTENT IMMUNO-ONCOLOGY PIPELINE IS TAKING SHAPE



WAVE 1


NMEs that complement our global brands

Hematologic Malignancies



TAK-924
FY21 target approval

Lung Cancer & Solid Tumors

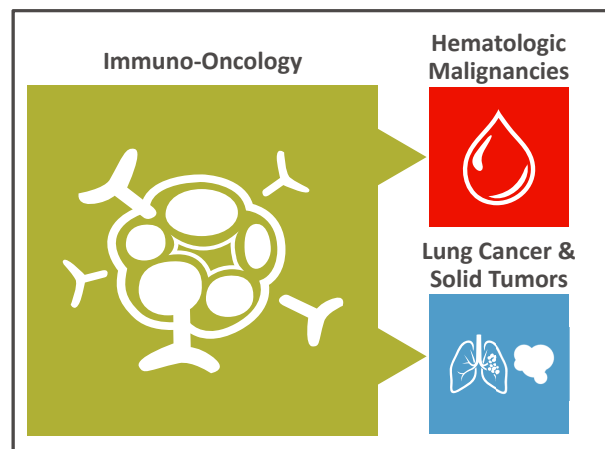


TAK-007
FY23 target approval

TAK-788
FY21 target approval

WAVE 2

Leading platforms in immuno-oncology and cell therapies



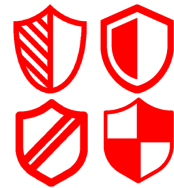


Unique Partnership Model



- Innovative, disruptive platforms
- Agility in 'open lab' model

Differentiated Portfolio

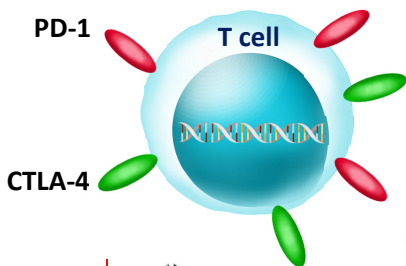


- Harness innate immunity
- Eye towards solid tumors

THE FIRST BREAKTHROUGHS IN CANCER IMMUNOTHERAPY TARGET T CELLS



T CELL CHECKPOINT INHIBITORS

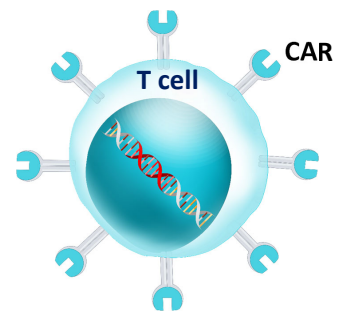


KEYTRUDA

OPDIVO
(nivolumab)

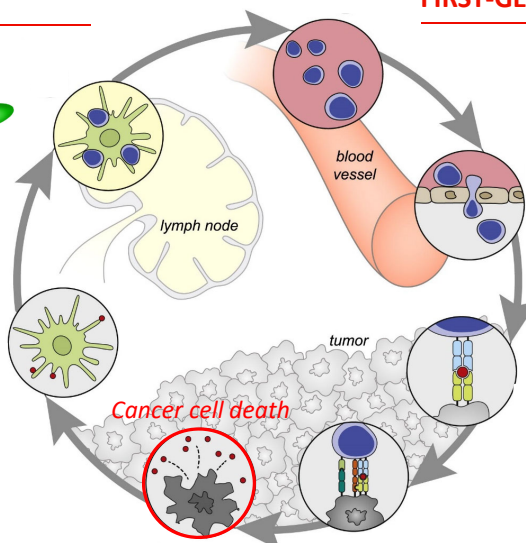
YERVOY
(ipilimumab)
Injection for intravenous use only

FIRST-GEN CAR-Ts

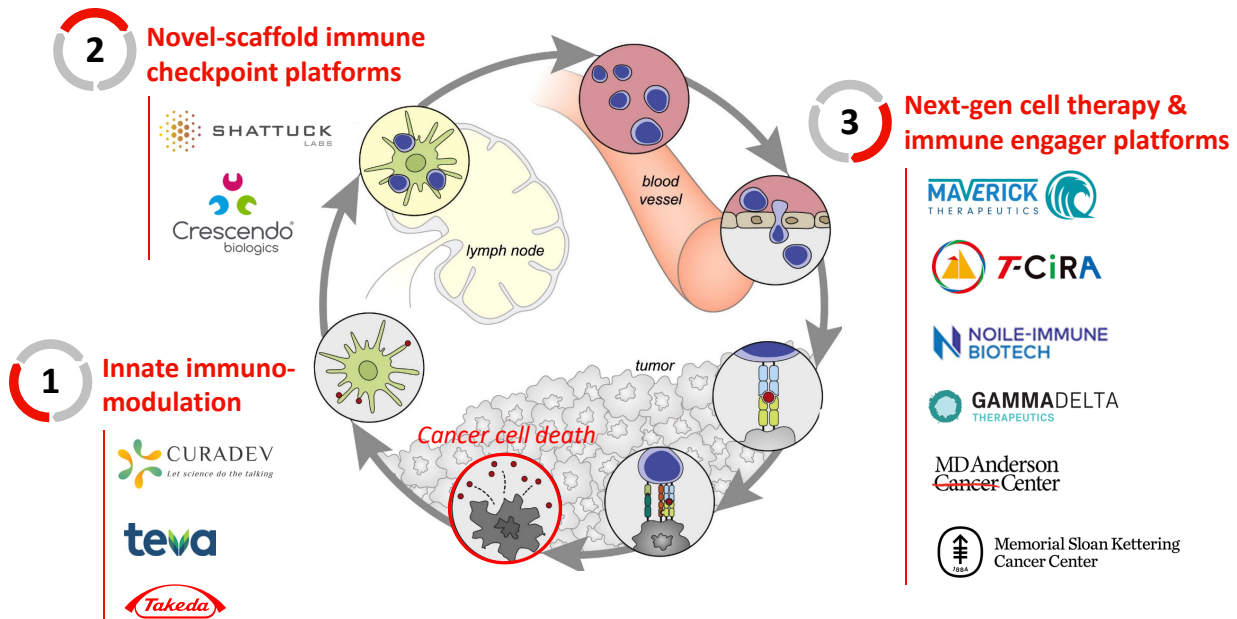


YESCARTA
(axicabtagene ciloleucel)

KYMRIAH
(tisagenlecleucel)
Suspension for IV infusion

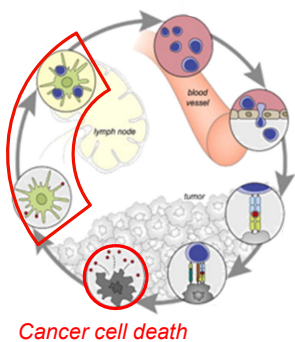


OUR FOCUS IS ON NOVEL MECHANISMS IN THE CANCER-IMMUNITY CYCLE



Adapted from Chen & Mellman, *Immunity* 2013

1 EMERGING STRENGTH IN TARGETED INNATE IMMUNE MODULATION



HIGH UNMET NEED	Patients refractory/ unresponsive to current immunotherapies
OUR DIFFERENTIATED APPROACH	Systemic therapies leveraging innate immunity to enhance response breadth, depth & durability

PLATFORM	PARTNER	MECHANISM-OF-ACTION	PROGRAMS	PRE-CLINICAL	PH 1
STING agonism	CURADEV <i>Let science do the talking</i>	• Innate-to-adaptive priming	TAK-676 (STING agonist) Targeted STING agonist	████████████████████ ████████████████████	
SUMOylation		• Innate immune enhancer	TAK-981 TAK-981 (ADCC combo)	████████████████████ ████████████████████	▶▶
Attenukine™	teva	• Targeted attenuated IFN-α	TAK-573 (CD38-Attenukine™) Next-gen Attenukine™	████████████████████ ████████████████████	▶▶

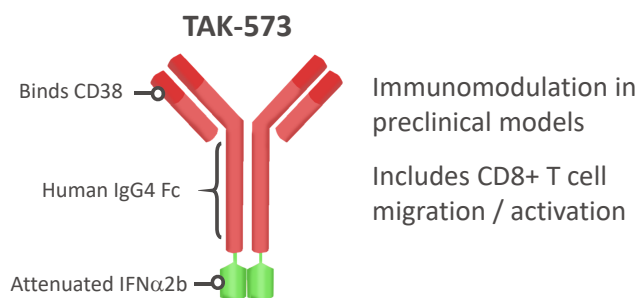
ADCC = Antibody-dependent cellular cytotoxicity

▶▶ = first-in-class

1 ATTENUKINE™ PLATFORM ELICITS BOTH DIRECT TUMOR KILL AND IMMUNE ACTIVATION

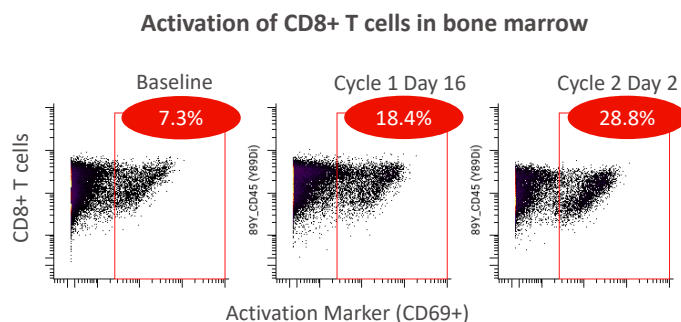


TARGETED ATTENUATED TYPE I IFN PAYLOAD



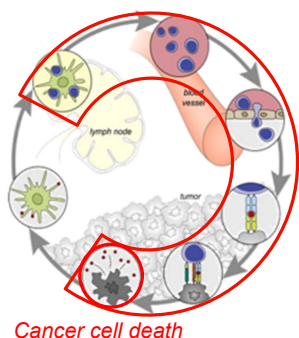
FPI = first patient in R/R MM = Relapsed / refractory multiple myeloma POM = proof-of-mechanism

TAK-573 POM IN ONGOING PHASE 1 R/R MM STUDY



EXPECTED MILESTONES (FY)	2019	2020
	Ph1 FPI in solid tumors	Ph1b MM (incl. combinations)

2 NOVEL SCAFFOLD NEXT-GENERATION CHECKPOINT MODULATORS



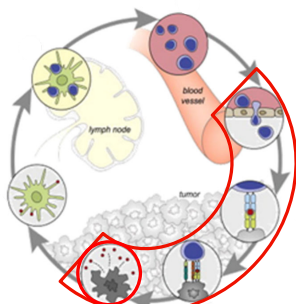
HIGH UNMET NEED	Current checkpoint modulators fail to improve overall survival in majority of patients
OUR DIFFERENTIATED APPROACH	New classes of checkpoint inhibitors designed to increase breadth and depth of responses

PLATFORM	PARTNER	MECHANISM-OF-ACTION	PROGRAMS	PRE-CLINICAL	PH 1
Humabody Vh	Crescendo biologics	• Unique pharmacology	Concept 1 Concept 2	██████████ ██████████	██████████ ██████████
Agonist-redirected checkpoints	SHATTUCK LABS	• Co-inhibition & co-stimulation	TAK-252 / SL-279352 (PD1-Fc-OX40L) TAK-254 / SL-115154 (CSF1R-Fc-CD40L)	████████████████████ ████████████████████	████████████████████ ████████████████████

Vh = Variable heavy domain

██████████ = first-in-class

3 BRINGING 5 NOVEL CELL THERAPY PLATFORMS TO THE CLINIC BY THE END OF FY20



Cancer cell death

HIGH UNMET NEED	Current CAR-T therapies have significant challenges & fail to address solid tumors
OUR DIFFERENTIATED APPROACH	Leverage novel cell platforms & engineering to address shortcomings in liquid & solid tumors

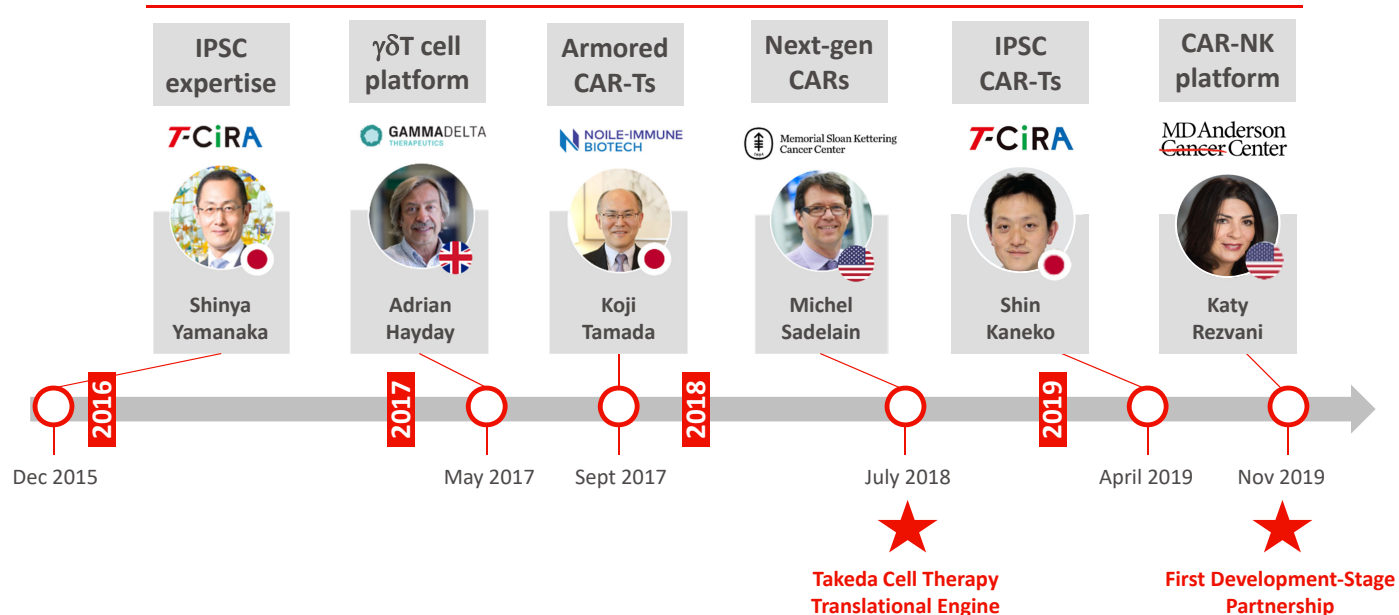
<p>INNATE IMMUNE PLATFORMS</p> <ul style="list-style-type: none"> • Multiple mechanisms of tumor killing • 'Off-the-shelf' • Utility in solid tumors 	<p>NK & $\gamma\delta$T cells</p> <p>Innate tumor sensors & effectors</p> <p>Engineered CAR</p> <p>Fc-mediated killing</p>
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NK = Natural killer

3 A NETWORK OF TOP INNOVATORS IS FUELING TAKEDA'S CELL THERAPY ENGINE



CUTTING-EDGE ENGINEERING & CELL PLATFORMS



IPSC = Induced pluripotent stem cell NK = Natural killer

Dr. Sadelain is a co-inventor on patents relative to next-gen CARs, intellectual property that MSK has licensed to Takeda. As a result of these licensing arrangements, Dr. Sadelain and MSK have financial interests related to these research efforts.

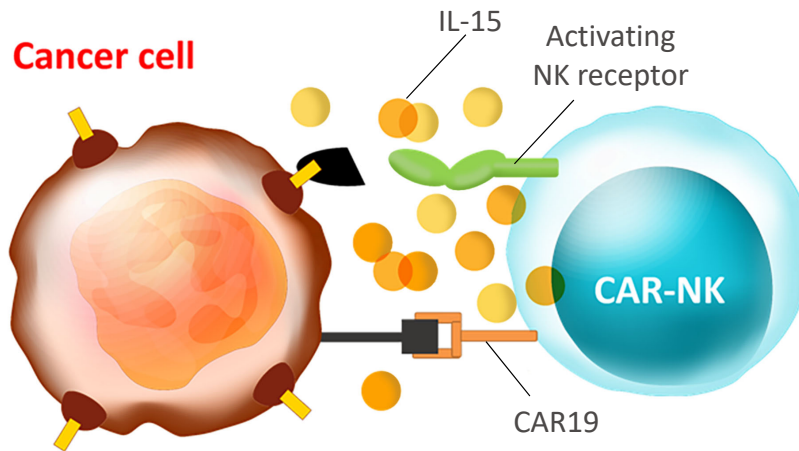
TAKEDA IS EMBARKING ON A TRANSFORMATIVE CAR-NK PARTNERSHIP THAT COULD ENTER PIVOTAL TRIALS IN 2021



NK CAR Platform

Multiple mechanisms of tumor killing

Potential of innate & adaptive immunity



FOUR NOVEL, OFF-THE-SHELF CAR-NK THERAPIES IN DEVELOPMENT



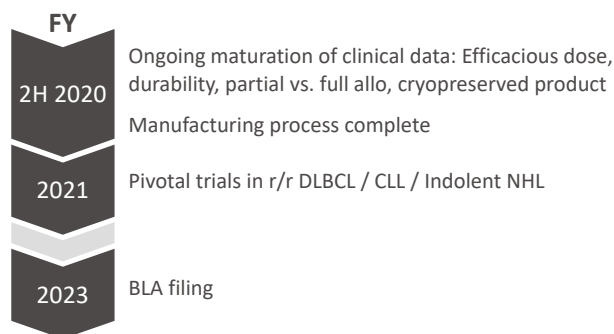
PATIENT VALUE PROPOSITION

Rapid and deep responses with a short-time-to-treatment, safe, off-the-shelf CAR-NK available in outpatient & community settings

Initial opportunity in G7 countries (CD19)*	
3L+ DLBCL	~8,000
3L+ CLL	~5,000
3L+ iNHL	~6,000

Potential to move into earlier lines of therapy

PLATFORM VALUE INFLECTIONS



PLATFORM	PARTNER	MECHANISM-OF-ACTION	PROGRAMS	PRECLINICAL	PH 1
CAR-NK (allo cord blood)	MD Anderson Cancer Center Dr. Katy Rezvani	• Non-autologous NK cell therapy	TAK-007 (CD19 CAR-NK) BCMA CAR-NK Platform expansion	████████████████████	████████████████████

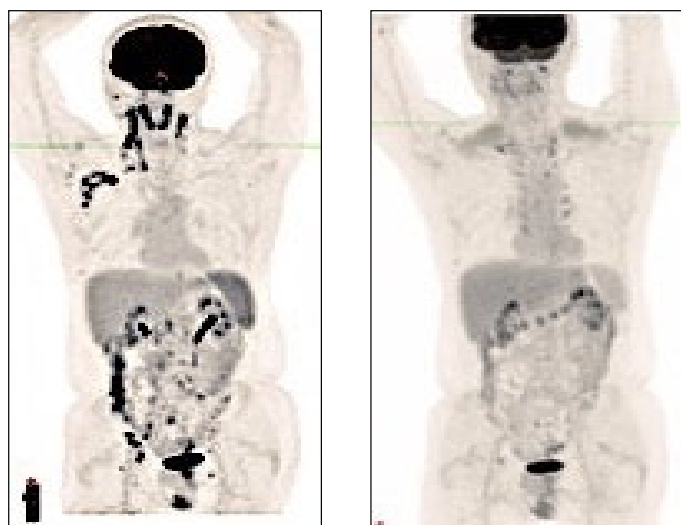
🚩 = first-in-class

CLL = Chronic lymphocytic leukemia DLBCL = Diffuse large B-cell lymphoma iNHL = Indolent non-Hodgkin's lymphoma
*Estimated number of patients projected to be initially eligible for treatment in G7 markets, subject to regulatory approval

3 DRAMATIC COMPLETE RESPONSE IN FIRST PATIENT TREATED

47-YEAR OLD MALE WITH RELAPSED TRANSFORMED DOUBLE-HIT (C-MYC / BCL-2) DLBCL

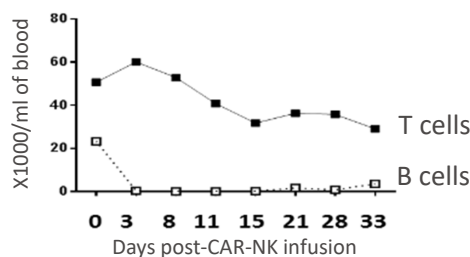
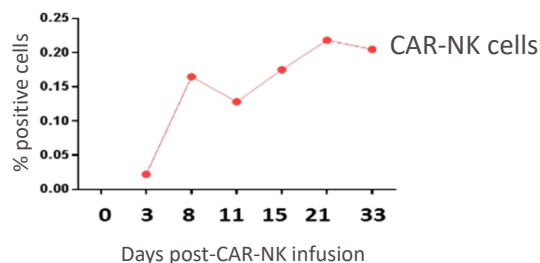
KINETICS OF CAR-NK VERSUS ENDOGENOUS T AND B CELLS IN PERIPHERAL BLOOD



Baseline scan

Day 30 post CAR19-NK

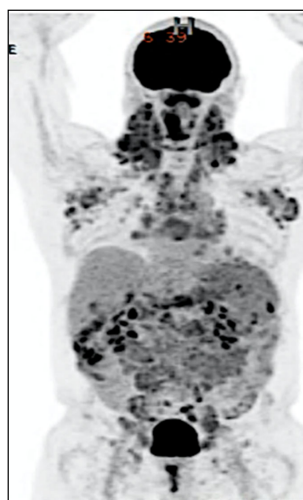
Data from Dr. Katy Rezvani, MD Anderson Cancer Center



3 IMPRESSIVE RESPONSES IN OTHER HEAVILY PRETREATED PATIENTS

61-YEAR OLD MALE CLL/RICHTER'S TRANSFORMATION (5 PRIOR LINES OF THERAPY)

60-YEAR OLD FEMALE WITH CLL / ACCELERATED CLL (5 PRIOR LINES OF THERAPY)



Baseline scan

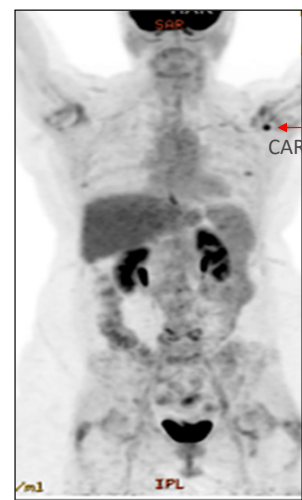


Day 30 post CAR19-NK

CR in Richter's; SD in CLL



Baseline scan



Day 30 post CAR19-NK

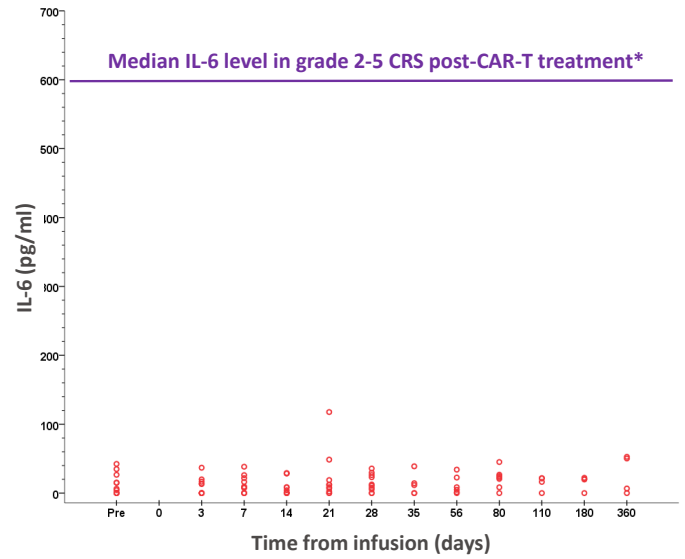
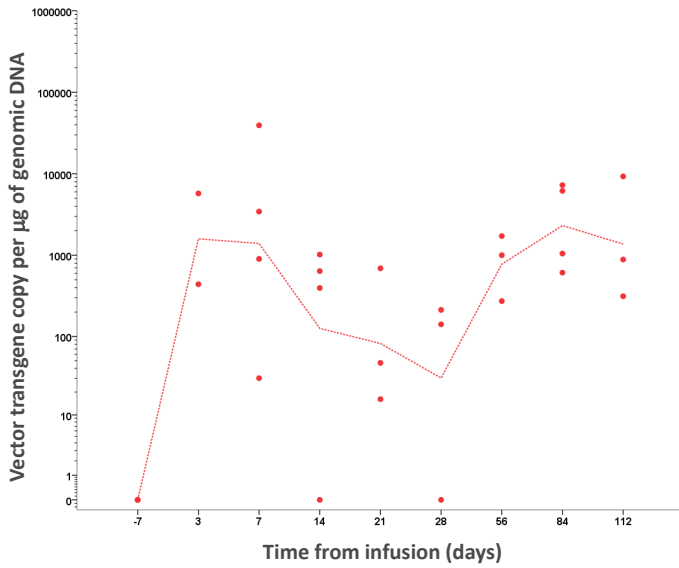
CLL = Chronic lymphocytic leukemia CR = Complete response SD = Stable disease
Data from Dr. Katy Rezvani, MD Anderson Cancer Center

3 CAR-NK CELLS PERSIST IN PATIENTS AND DO NOT TRIGGER CYTOKINE RELEASE SYNDROME (CRS)



CAR-NK CELLS PERSIST UP TO 4 MONTHS POST INFUSION

IL-6 LEVELS POST CAR-NK INFUSION DO NOT INDICATE CRS



CRS = Cytokine Release Syndrome
 *Turtle et al. 2017
 Data from Dr. Katy Rezvani, MD Anderson Cancer Center

3 CAR-NK EFFICACY & TOXICITY TREATING MULTIPLE DIAGNOSES



	Diagnosis	Lines of Treatment	HLA Match	CRS / Neurotox	Complete Response
Dose Level 1	DLBCL - Relapsed transformed double-hit	3 Incl. ASCT	Partial match	None	✓
	DLBCL - Refractory	7	Partial match	None	PD
	CLL	4 Incl. ibrutinib & venetoclax	Partial match	None	✓
Dose Level 2	CLL	4 Incl. ibrutinib	Partial match	None	PD
	CLL/Richter's transformation	5 Incl. ibrutinib	Partial match	None	✓* Richter's
	CLL/Accelerated CLL	5 Incl. ibrutinib & venetoclax	Partial match	None	✓
	CLL	4 Incl. ibrutinib	Partial match	None	✓
Dose Level 3	DLBCL - Refractory	11 Incl. ASCT	Partial match	None	✓
	DLBCL - Relapsed transformed double-hit	4 Incl. ASCT	Partial match	None	✓
	Follicular lymphoma - Relapsed	4 Incl. ASCT	Mismatch	None	PD
	Follicular lymphoma - Relapsed	4	Mismatch	None	✓

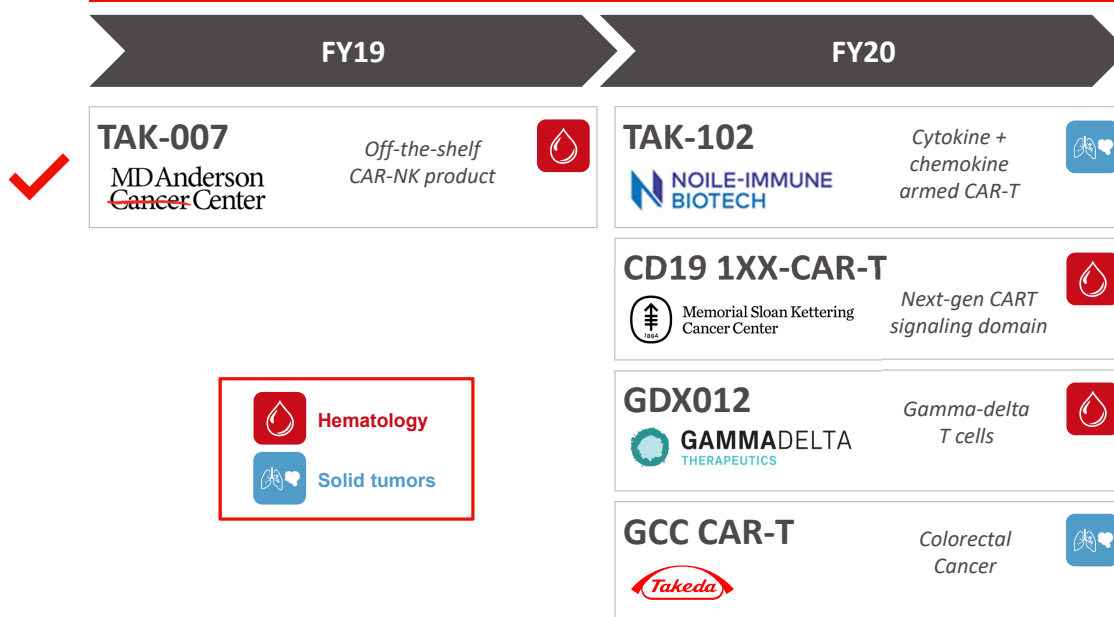
CLL = Chronic lymphocytic leukemia
 CRS = Cytokine release syndrome
 DLBCL = Diffuse large B-cell lymphoma
 ASCT = Autologous stem cell transplant
 HLA = Human leukocyte antigen
 PD = Progressive disease
 *Complete response for Richter's

Data from Dr. Katy Rezvani, MD Anderson Cancer Center

3 FAST-TO-CLINIC CELL THERAPY ENGINE WILL MAXIMIZE LEARNINGS ON MULTIPLE 'DISRUPTIVE' PLATFORMS



5 CLINICAL-STAGE PROGRAMS EXPECTED BY END OF FY20



FY21+: Other cell therapy candidates

3 A RICH AND POTENTIALLY TRANSFORMATIVE EARLY CLINICAL ONCOLOGY PIPELINE



PLATFORM	PARTNER(S)	MECHANISM-OF-ACTION	PROGRAMS	PRECLINICAL	PH1
STING agonism	CURADEV	Innate-to-adaptive priming	TAK-676 (STING agonist) Targeted STING agonist	██████████	██████████
SUMOylation		Innate immune enhancer	TAK-981 TAK-981 (ADCC combo)	██████████	██████████
Attenukine™	teva	Targeted attenuated IFN-α	TAK-573 (CD38-Attenukine™)	██████████	██████████
Agonist-redirected checkpoints	SHATTUCK LABS	Co-inhibition & co-stimulation	TAK-252 / SL-279353 TAK-254 / SL-115154	██████████	██████████
Shiga-like toxin A	tem	Novel cytotoxic payload	TAK-169 (CD38-SLTA)	██████████	██████████
IGN toxin	immun.gen	Solid tumor-targeted ADC	TAK-164 (GCC-ADC)	██████████	██████████
Conditional T cell engagers	MAVERICK THERAPEUTICS	Novel solid tumor platform	MVC-101 (EGFR COBRA™)	██████████	██████████
Cell therapy platforms	Memorial Sloan Kettering Cancer Center, NOILE-IMMUNE BIOTECH, MD Anderson Cancer Center, GAMMADELTA THERAPEUTICS	Off-the-shelf cell therapies	TAK-007 (CD19 CAR-NK) 5 cell therapies expected in clinic by end of FY20	██████████	██████████

UNDISCLOSED TARGETS

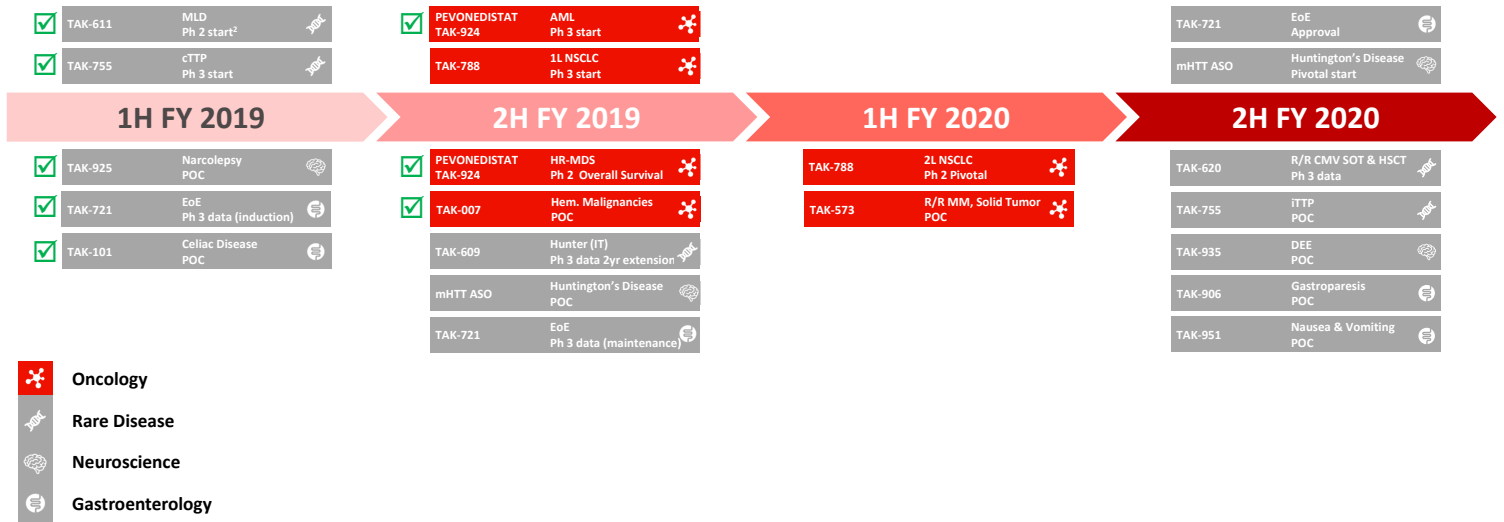
➤ = first-in-class

Hematology Solid tumors

NME MILESTONES ACHIEVED IN FY19 AND LOOKING AHEAD TO OTHER POTENTIAL MILESTONES¹ THROUGH FY20



PIVOTAL STUDY STARTS, APPROVALS



✓ Denotes milestones that have been achieved.

KEY DATA READOUTS

1. Potential key milestone dates as of November 14, 2019. The dates included herein are estimates based on current data and are subject to change
 2. Potentially registration enabling

SUMMARY



1

Total transformation of preclinical & early clinical pipeline

2

Differentiated opportunities in IO leveraging innate immunity & cell therapies

3

Multiple near-term catalysts informing momentum towards solid tumors