

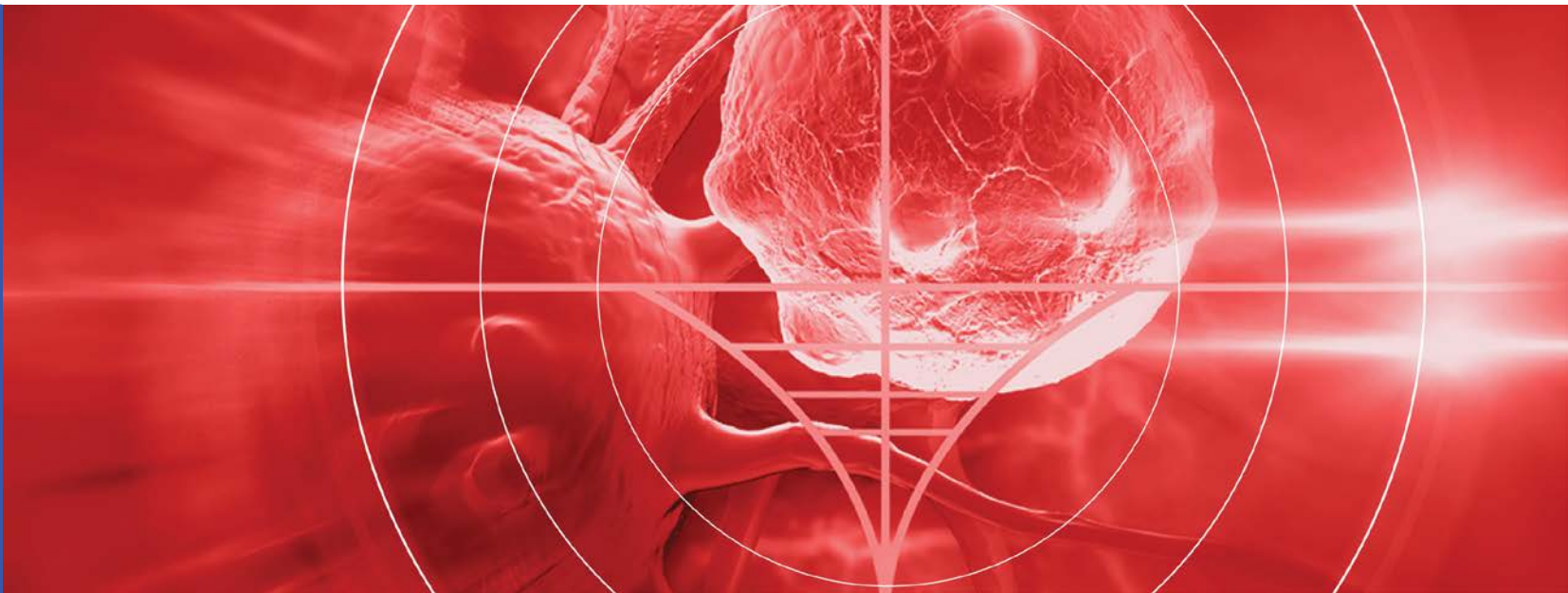
# ADAPTIMMUNE INVESTOR PRESENTATION 2016

June 28, 2016



Adaptimmune

TRANSFORMING T CELL THERAPY



## DISCLAIMER

This presentation contains “forward-looking statements,” as that term is defined under the Private Securities Litigation Reform Act of 1995 (PSLRA), which statements may be identified by words such as “believe,” “may,” “will,” “estimate,” “continue,” “anticipate,” “intend,” “expect” and other words of similar meaning. These forward-looking statements involve certain risks and uncertainties. Such risks and uncertainties could cause our actual results to differ materially from those indicated by such forward-looking statements, and include, without limitation: the success, cost and timing of our product development activities and clinical trials; our ability to submit an IND and successfully advance our technology platform to improve the safety and effectiveness of our existing TCR therapeutic candidates; the rate and degree of market acceptance of T-cell therapy generally and of our TCR therapeutic candidates; government regulation and approval, including, but not limited to, the expected regulatory approval timelines for TCR therapeutic candidates; and our ability to protect our proprietary technology and enforce our intellectual property rights; amongst others. For a further description of the risks and uncertainties that could cause our actual results to differ materially from those expressed in these forward-looking statements, as well as risks relating to our business in general, we refer you to our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on May 12, 2016 and our other SEC filings.

We urge you to consider these factors carefully in evaluating the forward-looking statements herein and are cautioned not to place undue reliance on such forward-looking statements, which are qualified in their entirety by this cautionary statement. The forward-looking statements contained in this presentation speak only as of the date the statements were made and we do not undertake any obligation to update such forward-looking statements to reflect subsequent events or circumstances. We intend that all forward-looking statements be subject to the safe-harbor provisions of the PSLRA.

# ADAPTIMMUNE

## LEADING THE TCR T-CELL SPACE

- Creating a pipeline of **SPEAR™** (Specific Peptide Enhanced Affinity Receptor) T-cells to treat solid tumors
- Three open INDs for the following SPEAR T-cells:
  - NY-ESO
    - ◆ 60% response rate already achieved at target dose in synovial sarcoma, a solid tumor
    - ◆ 91% response rate in multiple myeloma in combination with ASCT
    - ◆ Breakthrough and orphan drug status (US); positive COMP opinion on orphan status (Europe)
  - MAGE-A10
    - ◆ NSCLC - open
    - ◆ Bladder, melanoma, urothelial in site review
  - AFP for hepatocellular cancer
- Next IND expected for MAGE-A4 in 2017

## LEADING THE TCR T-CELL SPACE (CONTINUED)

- Precision engineering critical to achieve optimum affinity
  - Patented phage display system
- Target identification essential
  - Mass spec system up and running
  - Recently applied for patents on over 60 targets
- Long term persistence of T-cells key to efficacy
  - 3 years + achieved due to proprietary manufacturing method when pre-conditioning appropriate
    - ♦ 10-year supply agreement signed June 2016
- Second generation T-cell program in progress: goal of enhancing efficacy
  - First IND expected 2017
- Combination study planned for 2016

## RECENT DATA

### ASCO / ADAPTIMMUNE ANALYST AND INVESTOR DAY

- Demonstrate the importance of pre-conditioning
  - Excellent response rates in sarcoma (CTX and FDR)
  - No responses to date in third cohort of sarcoma (CTX alone)
  - No responses in ovarian, melanoma (CTX alone)
    - ◆ Protocols being revised; melanoma combination trial in planning
  - Persistence much longer (21 months to 3 years+) with appropriate pre-conditioning
    - ◆ Poorer expansion and persistence with just CTX
- Though differences in patient populations, incidence of CRS lower in frequency and severity than reported\* with CD19 CAR-T therapy
  - 53 patients treated (as of 1/27/16)
  - 8 CRS events in total
    - ◆ One grade 4, three grade 3, three grade 2, one grade 1





## BUILDING A PIPELINE

# BUILDING A PIPELINE

## ONGOING PROGRAMS FOR NY-ESO

INDICATION	RESEARCH	PRE-IND	PHASE I/II	STATUS
Synovial Sarcoma	Cohort 1: High NY-ESO expression, 12 patients			Complete
	Cohort 2: Low NY-ESO expression, 10 patients			Enrolling
	Cohort 3: Removal of fludarabine, 10 patients			Enrolling
	Cohort 4*: Modified CTX / fludarabine, 10 patients			Opening 2016
Multiple Myeloma	Autologous SCT, 25 patients (Rapoport Nat Med, 2015)			Complete
	Combination study, no auto SCT; 2 cohorts			In planning
Ovarian	10 patients			Enrolling
Melanoma	6 patients			Enrolling; potential for combination study
Non-small cell lung cancer	10 patients, Stage IIIb / IV NSCLC			Initiated Q4 2015
Investigator Initiated studies	NCI: synovial sarcoma (16 patients) and melanoma (13 patients)			Complete
	ATTACK: Esophageal: 12 patients			Active; recruitment to resume

\*Pending analysis of cohort 3

# BUILDING A PIPELINE

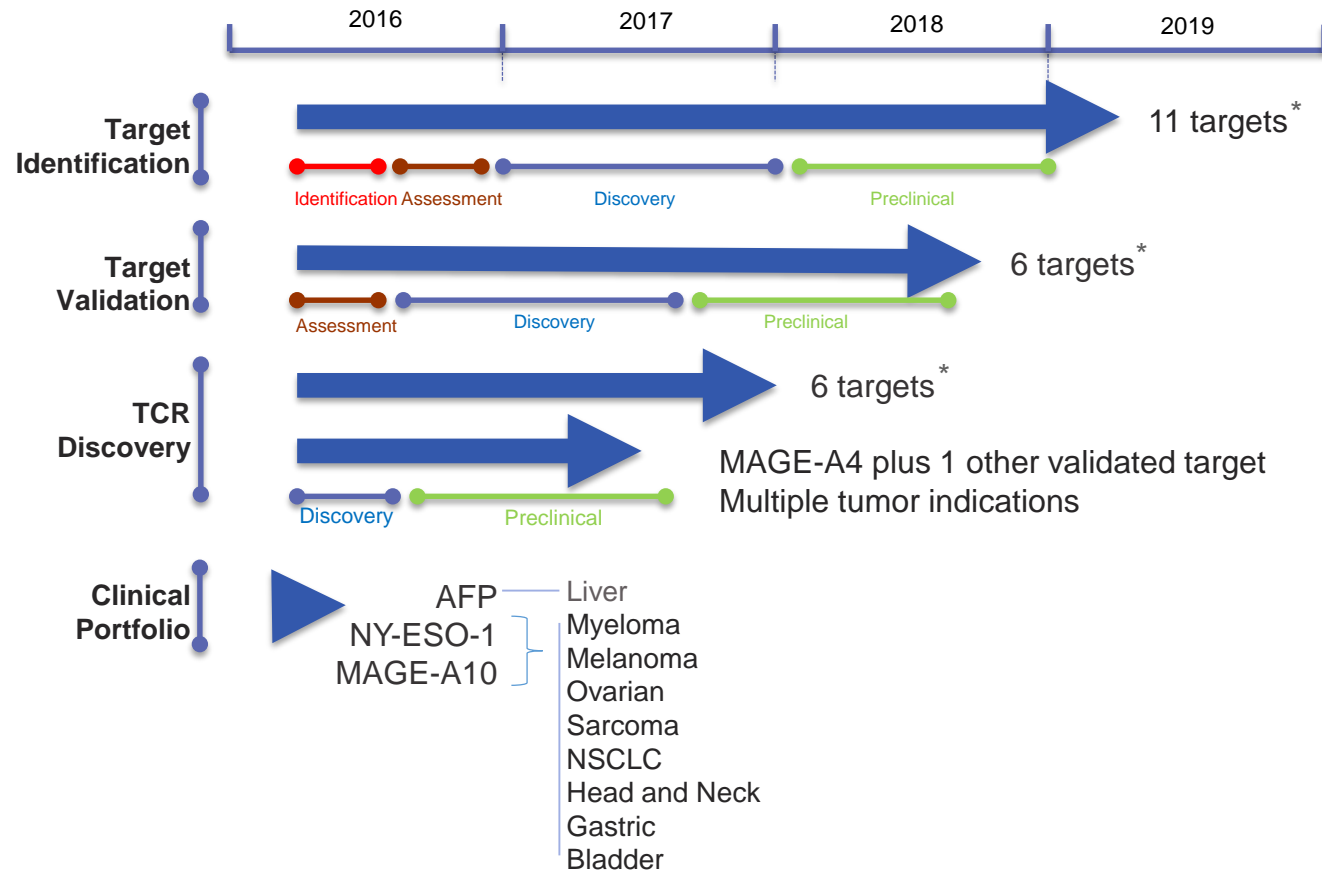
## DEEP PIPELINE OF WHOLLY-OWNED SPEAR T-CELLS AND TCRs

INDICATION	RESEARCH	PRE-IND	PHASE I/II	STATUS
Non-Small Cell Lung Cancer (NSCLC)	MAGE-A10 SPEAR T-cell			Initiated Q4 2015
Urothelial Melanoma Head and neck	MAGE-A10 SPEAR T-cell			Initiate in 2016
Hepatocellular cancer	AFP SPEAR T-cell			IND open; enrollment in 2016
Multiple cancer types	MAGE-A4 SPEAR T-cell			RAC and IND submission in 2017
Multiple cancer types	Generation 2 and 3 TCRs			INDs in 2017+
Multiple cancer types	Undisclosed			INDs from 2017+



# BUILDING A PIPELINE

## MULTIPLE INDs FROM 2017 ONWARDS (TARGETS AND NEXT GENERATION)



- All programs are run under Adaptimmune-owned INDs
- Next generation programs not represented on this chart

## BUILDING A PIPELINE

### BROAD COVERAGE OF MANY CANCERS WITH ADAPTIMMUNE'S EXISTING TCR PIPELINE

Indication	Frequency (%)			
	NY-ESO-1	MAGE-A10	MAGE-A4	Expression by 1 or more
Lung Squamous Cell	26	33	64	69
Bladder Cancer	26	31	38	50
Cutaneous Melanoma	32	29	23	48
Head and Neck	11	14	44	46
Ovarian Cancer	13	12	38	44
TN breast cancer	19	10	26	35
Endometrial Cancer	7	7	17	21
Esophageal Cancer	11	18	36	40
Gastric and Esophageal Cancer	11	17	32	35
Lung Adenocarcinoma	12	10	12	19
Cervical Cancer	4	7	23	26
Breast Cancer (all)	5	3	7	11

≥30%

20-30%

≥ 45%

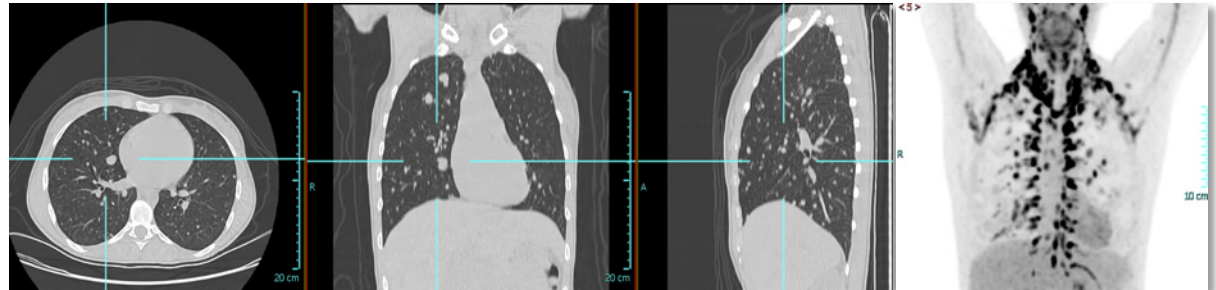


## SYNOVIAL SARCOMA: DATA AND PATH TO BLA

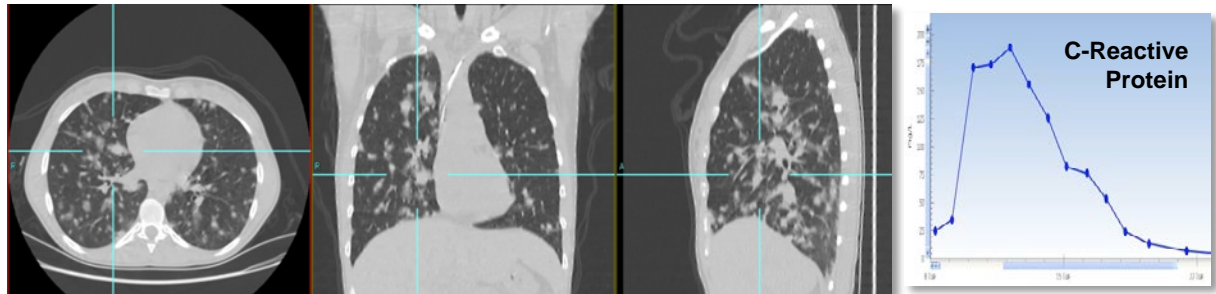
## PHASE I/II STUDY IN SYNOVIAL SARCOMA

### RADIOGRAPHIC PSEUDOPROGRESSION AND RESPONSE OF LUNG METASTASES LEADING TO COMPLETE RESPONSE

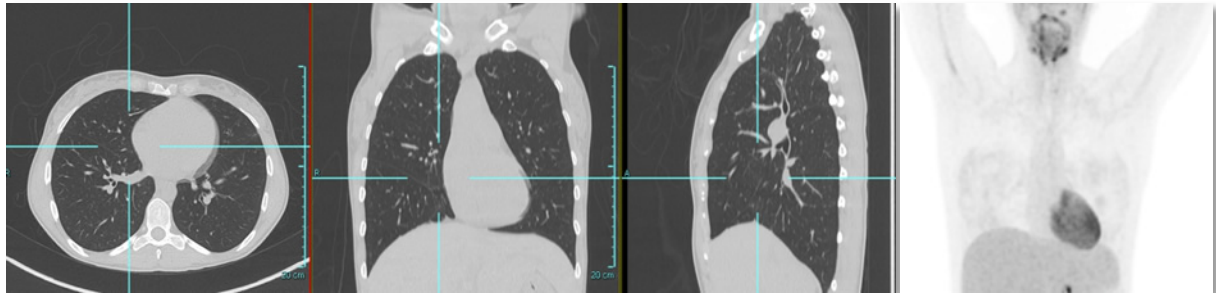
**Baseline:**  
Bilateral miliary  
metastatic disease



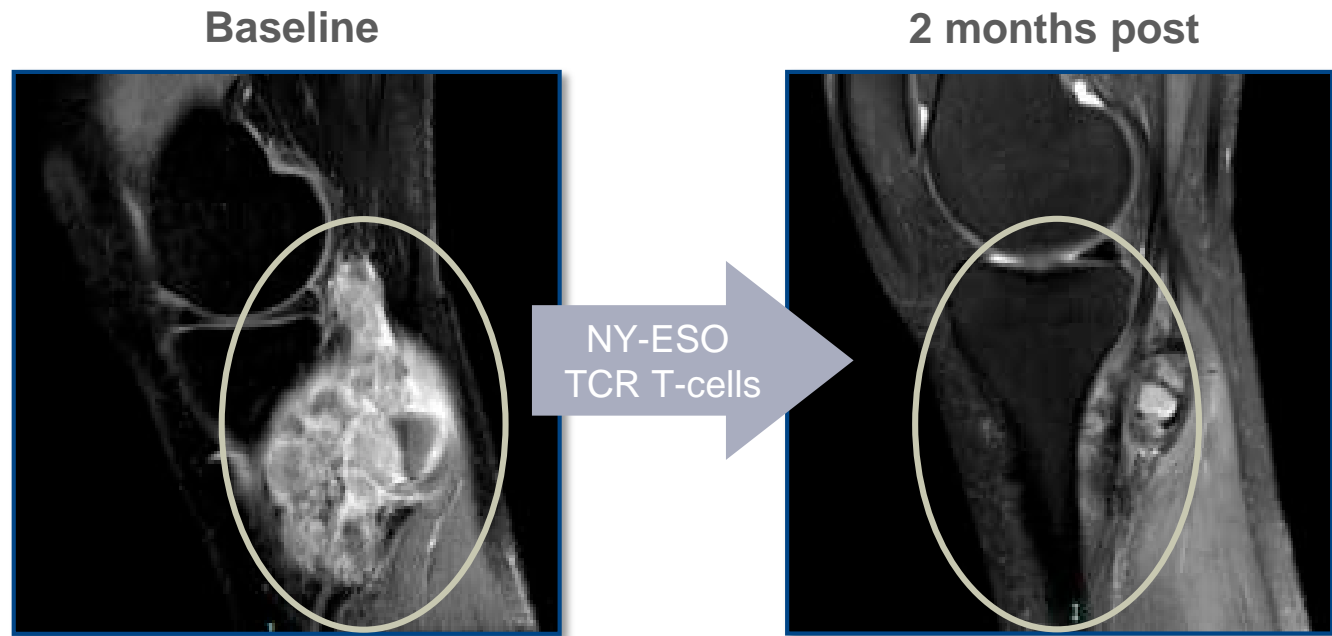
**Day +2:**  
Pseudoprogession  
due to immune  
infiltration



**Day +101:**  
Complete  
Response



# NEAR COMPLETE RESPONSE TO NY-ESO-1 T-CELLS OF UNRESECTABLE PRIMARY TUMOR IN THE KNEE

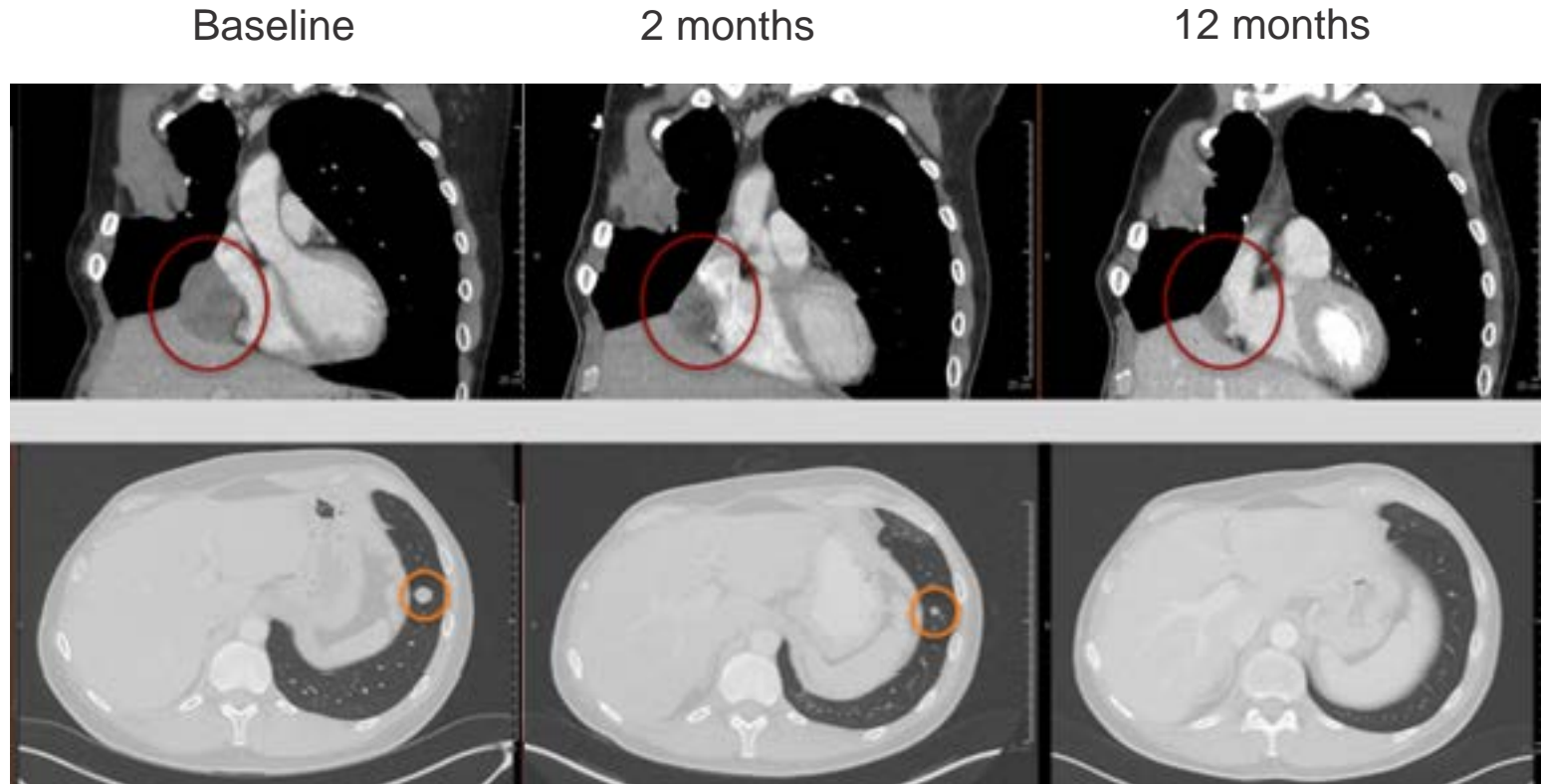


- Complete surgical resection accomplished, no irradiation
- Local disease remained controlled; patient developed lung metastasis with loss of NY-ESO-1



# TUMOR SHRINKAGE OVER THE COURSE OF SEVERAL MONTHS FOLLOWING NY-ESO-1 TCR FOR SYNOVIAL SARCOMA

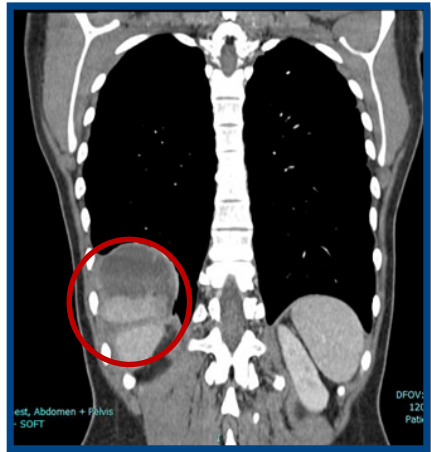
MULTIPLY RECURRENT, UNRESECTABLE PULMONARY MASSES



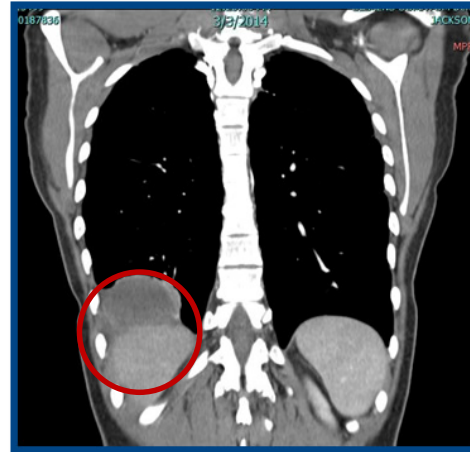
Ongoing PR 400+ days post T-cell infusion



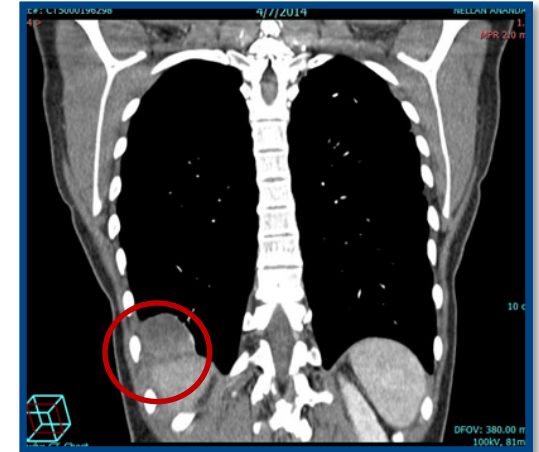
# CLINICAL RESPONSE FOLLOWED BY RESECTION AT PROGRESSION



1/22/14



3/3/14



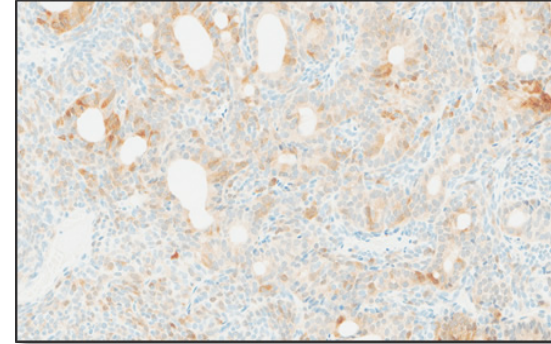
4/7/14

- Mass began to show regrowth ~6 months
- Surgically resected at 7 months
  - No NY-ESO-1 TCR cells found in tumor
  - Substantial CD4+ T-cells

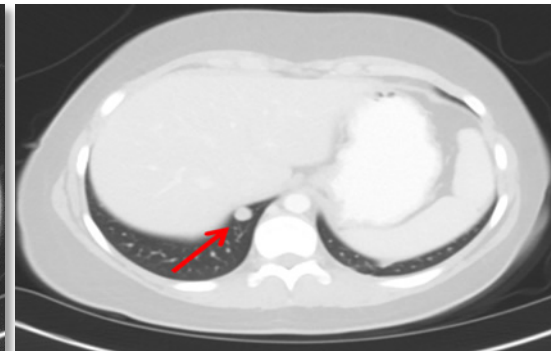
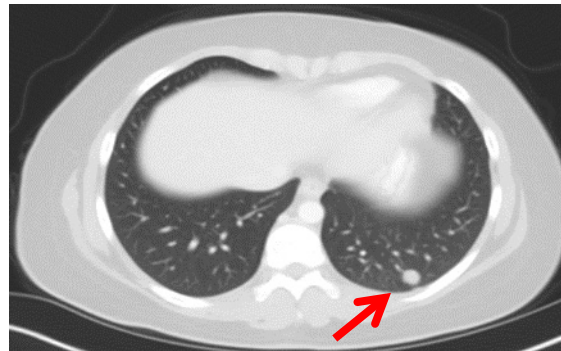
No evidence of disease 27 months post NY-ESO-1 T-cell infusion;  
20 months from surgical resection of metastasis

# CLINICAL RESPONSES OBSERVED ACROSS A SPECTRUM OF NY-ESO-1 EXPRESSION

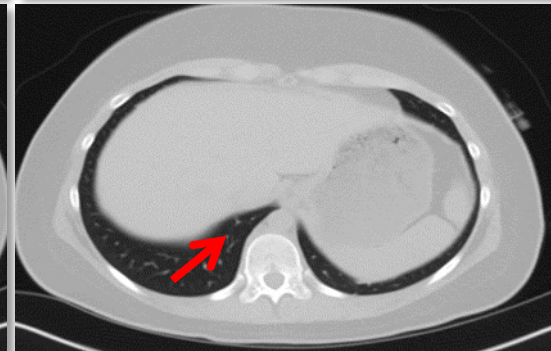
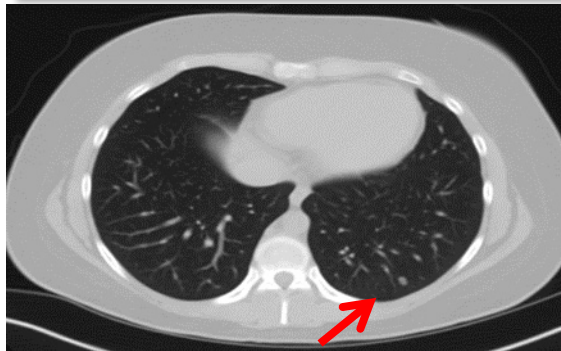
## RESPONSE IN A PATIENT WITH LOW NY-ESO-1 EXPRESSION



Baseline  
11-05-13

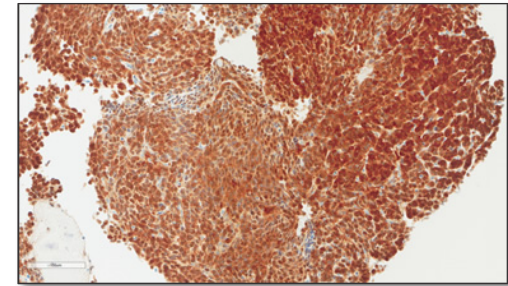


Month 3  
02-18-14

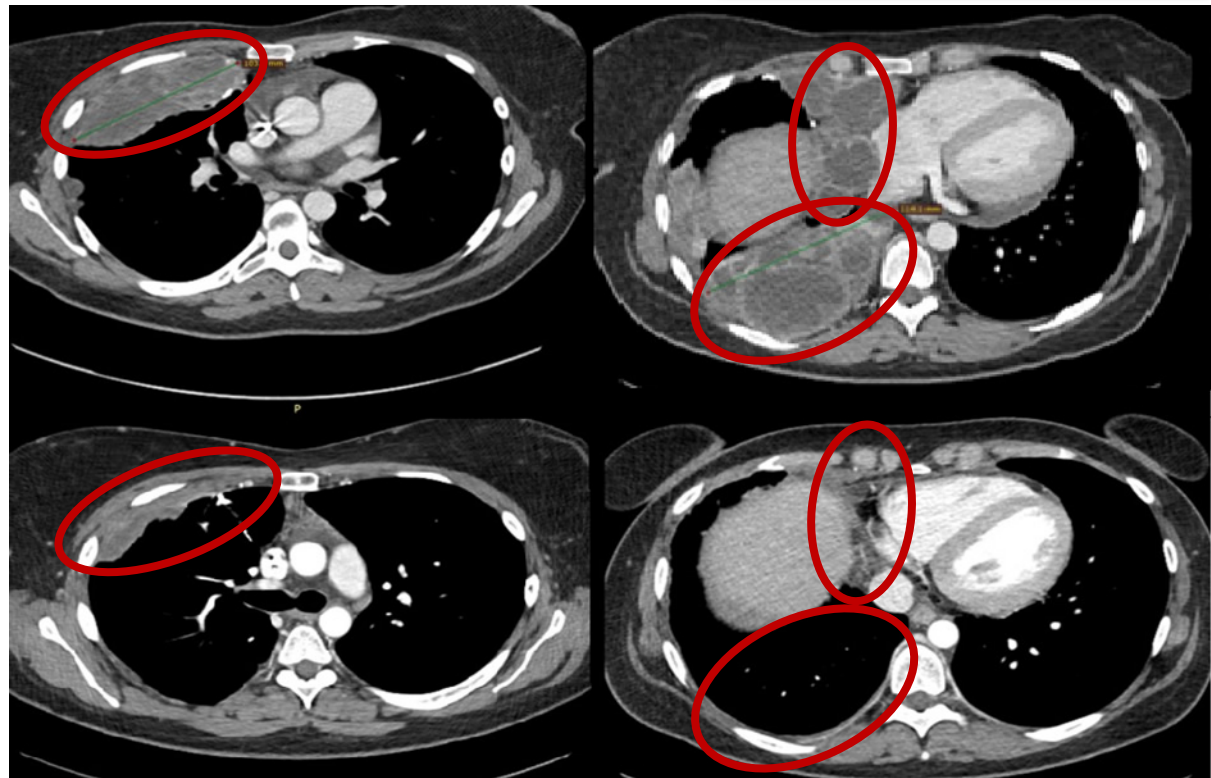


# CLINICAL RESPONSES OBSERVED ACROSS A SPECTRUM OF NY-ESO-1 EXPRESSION

## RESPONSE IN A PATIENT WITH VERY HIGH NY-ESO-1 EXPRESSION



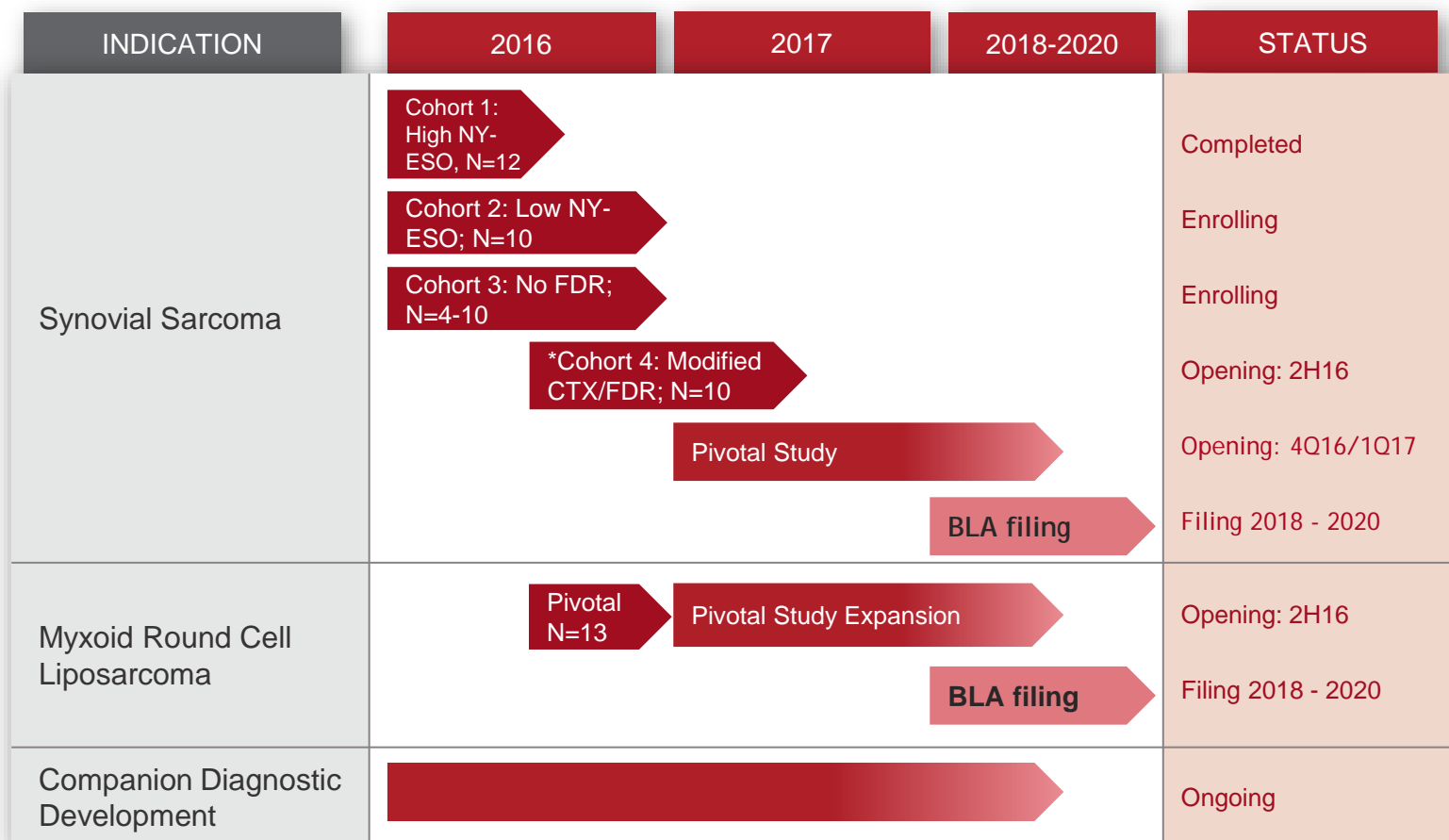
Baseline



Month 6

# NY-ESO CLINICAL PROGRAM: REGISTRATION PLAN IN SARCOMA

## BREAKTHROUGH & US ORPHAN DESIGNATION GRANTED



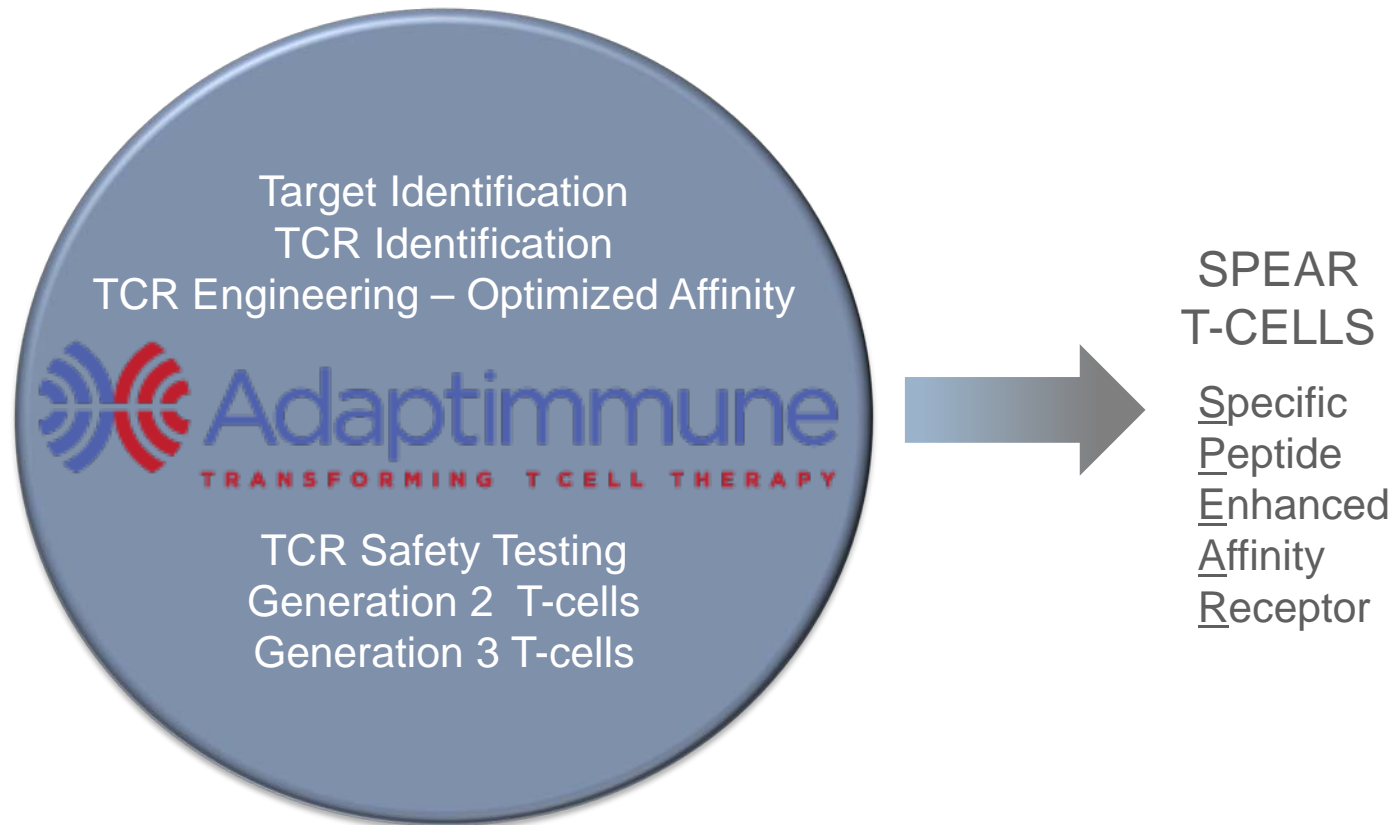




**THE SPEAR™ T-CELL**

# ADAPTIMMUNE SPEAR™ T-CELL PLATFORM

UNIQUELY ADDRESSING TARGET IDENTIFICATION, TCR AFFINITY & SAFETY



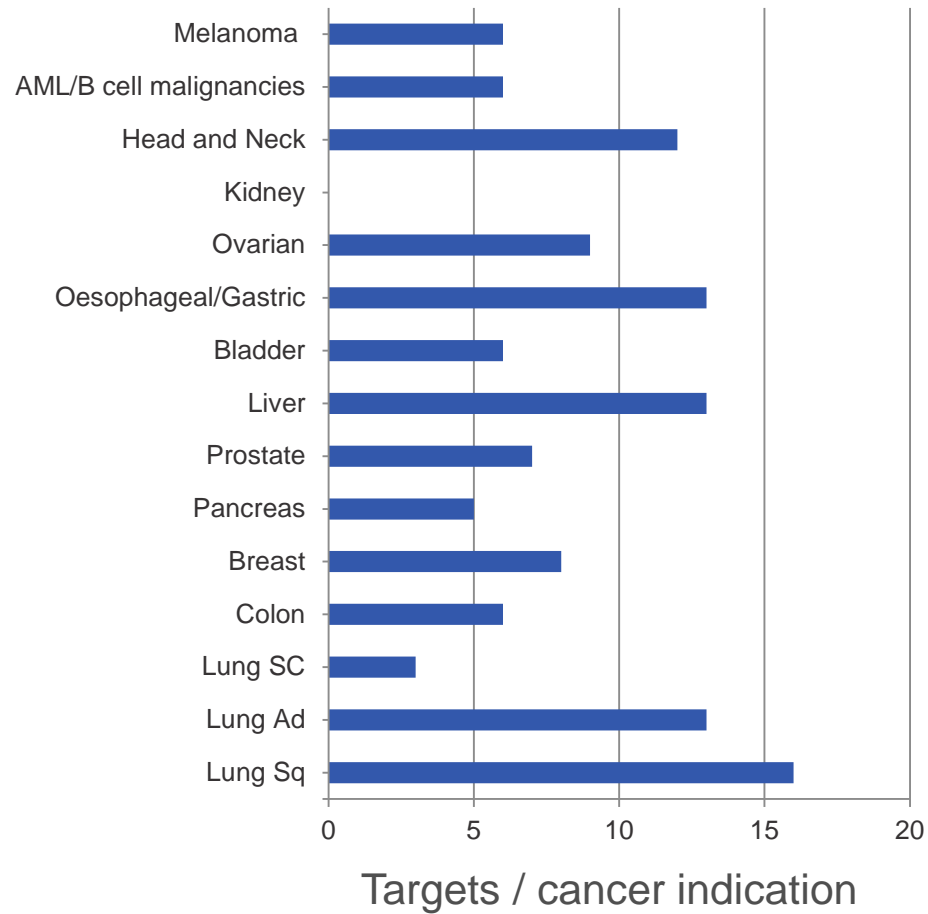


# PEPTIDE TARGET VALIDATION VIA MASS SPECTROMETRY

## FINDING THE RIGHT PEPTIDE TARGET

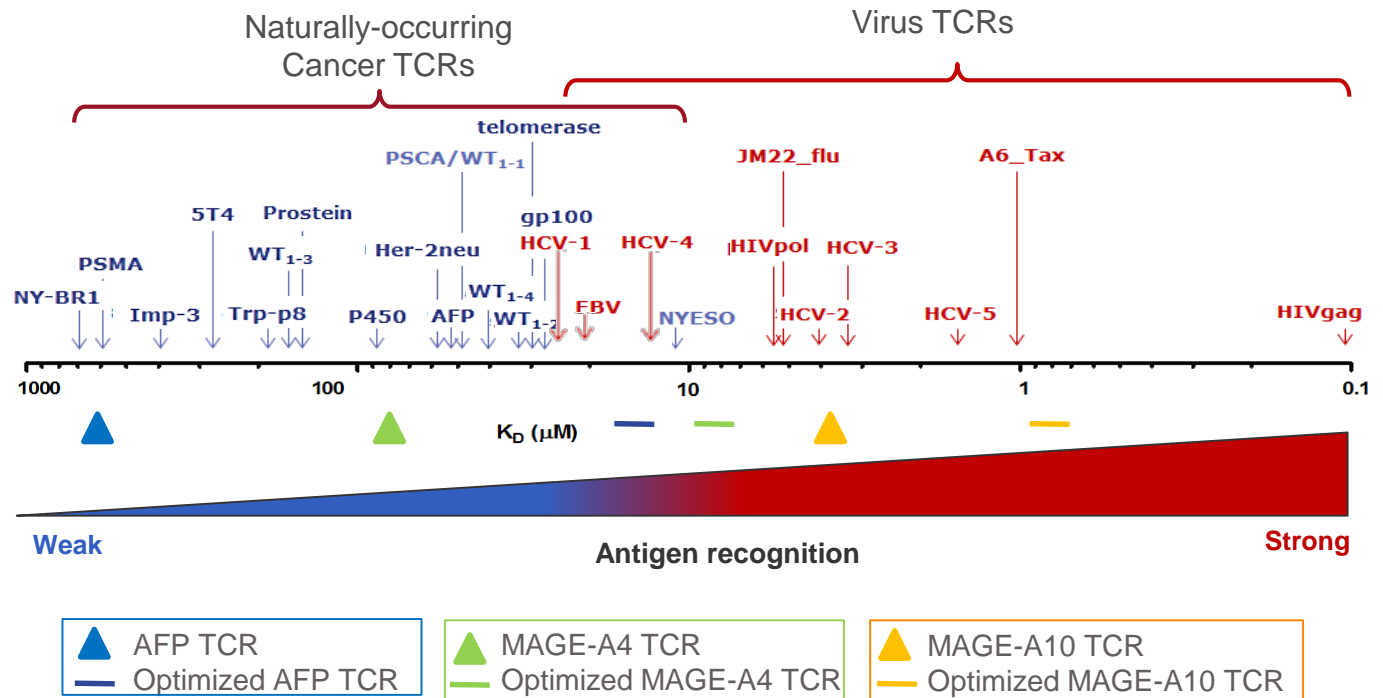
- Many identified target peptides fail to be presented *in vivo*
  - PSCA 14-22 (ALQPGTALL)
  - WT1 126-134 (RMFPNAPYL)
  - Telomerase 540-548 (ILAKFLHWL)
    - ◆ Not found by Adaptimmune mass spectrometry
    - ◆ Not detected by potent TCRs / T-cells
- Adaptimmune **ONLY** considers peptides to be validated if detected by mass spectrometry
  - Currently ~ 660,000 unique peptides within our databases

## RECENTLY FILED PATENTS ON OVER 60 TARGETS



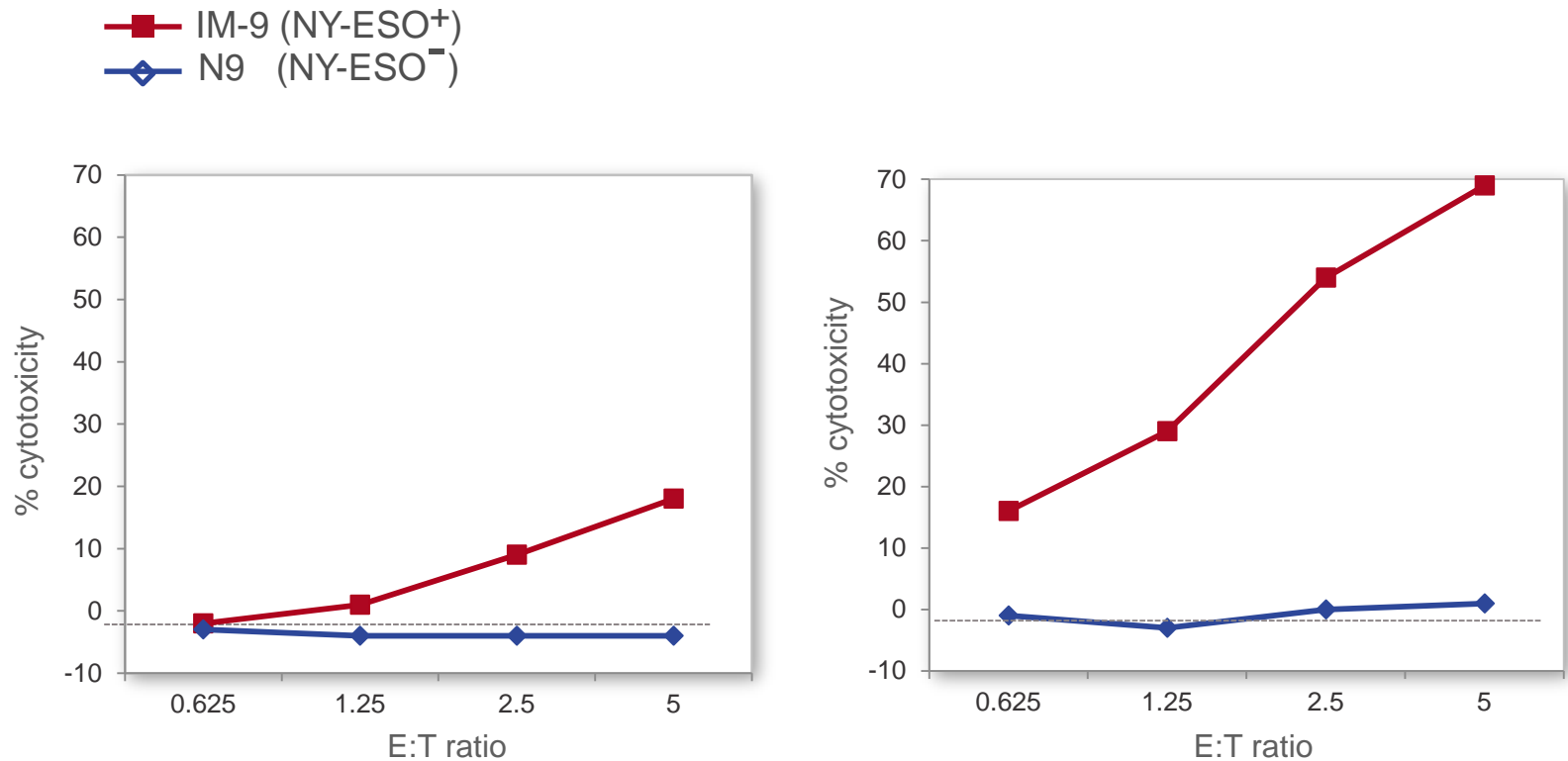
# AFFINITY OPTIMIZATION IS CRITICAL IN ALL CASES SO FAR

INDEPENDENT OF STARTING AFFINITY, OPTIMIZATION IS ESSENTIAL



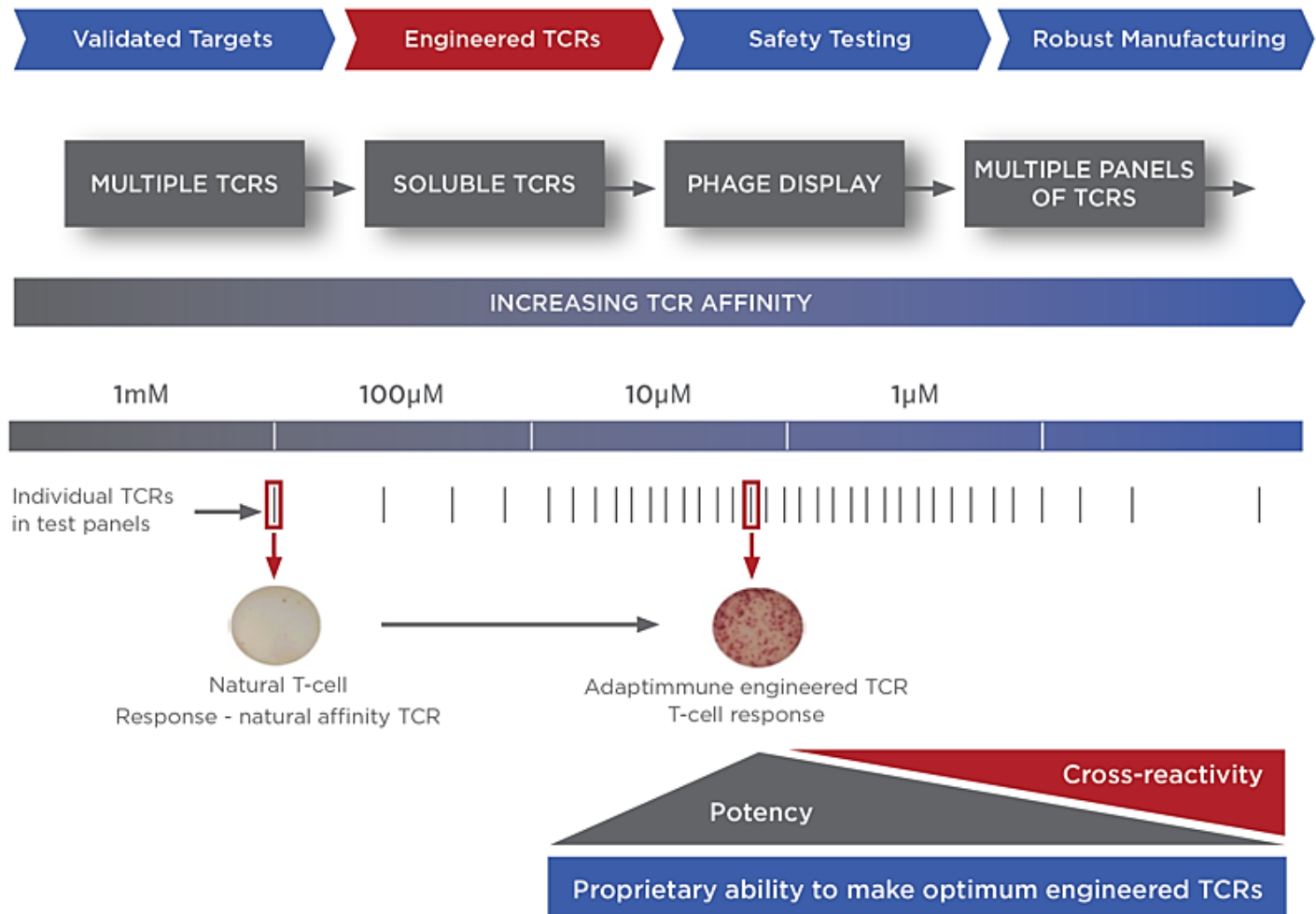
- Multiple parental TCRs allows selection of the most specific TCR
- The ideal affinity is different for each TCR and not possible to predict

# NY-ESO: NATURAL VERSUS ENGINEERED TCR FUNCTIONALITY

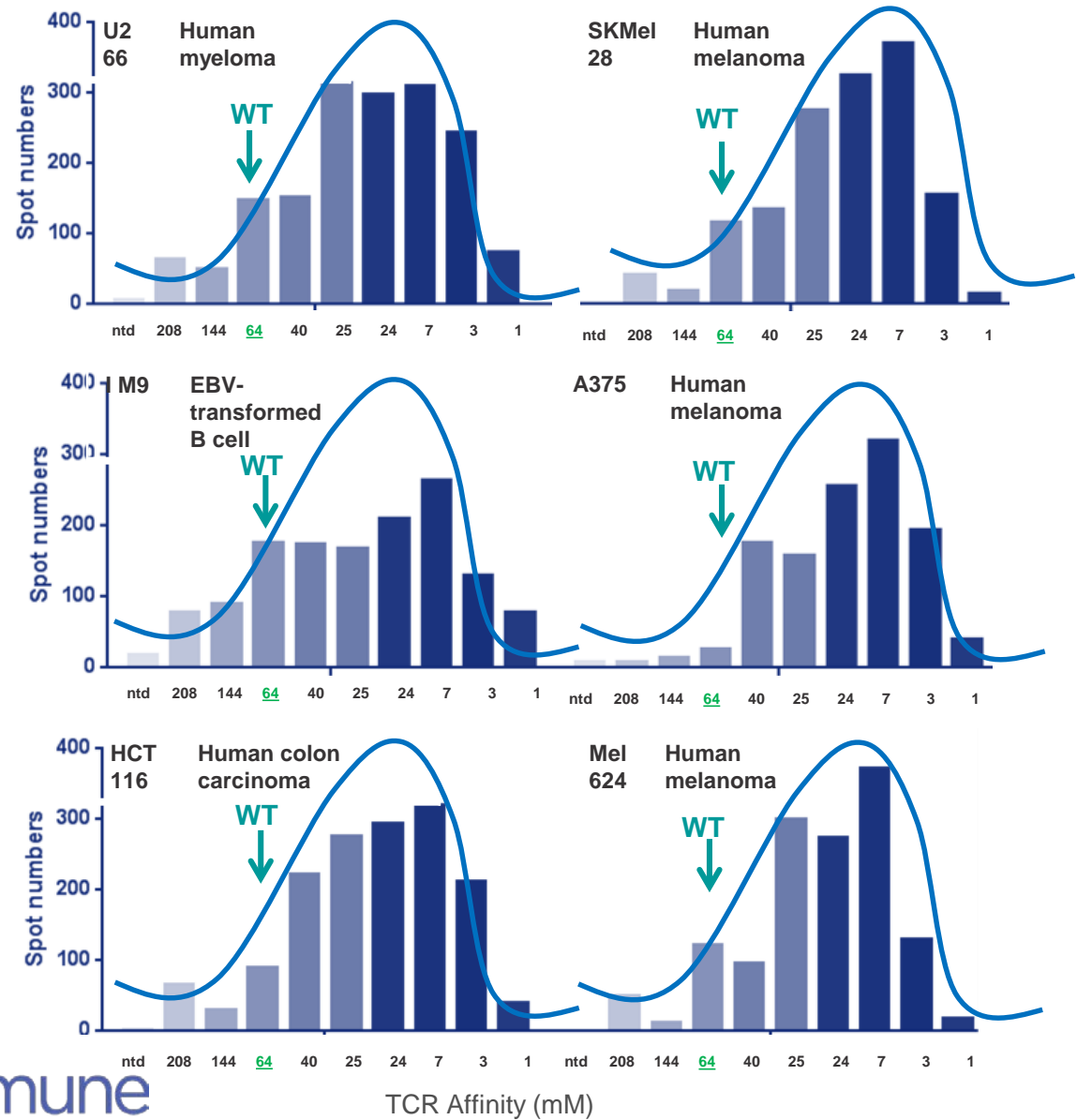


Even for NY-ESO, affinity engineering improves cancer killing

# FINDING THE RIGHT TCR AFFINITY



# MAGE-A4: EFFECT OF OPTIMIZING TCR AFFINITY

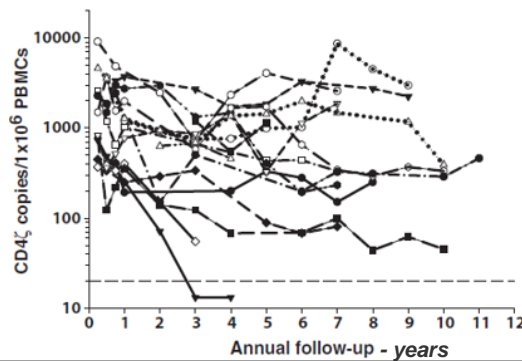




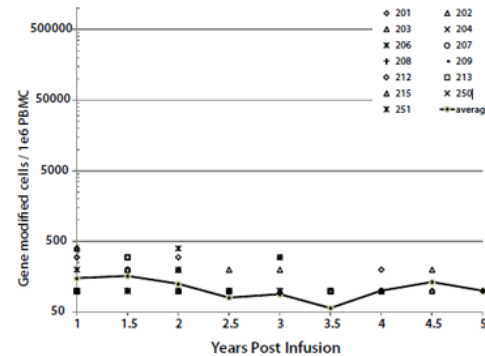
# MANUFACTURING CRITICAL TO PERSISTENCE AND QUALITY OF SPEAR T-CELLS

## CD3/CD28 BEAD METHOD PRODUCES LONG TERM PERSISTING T-CELLS

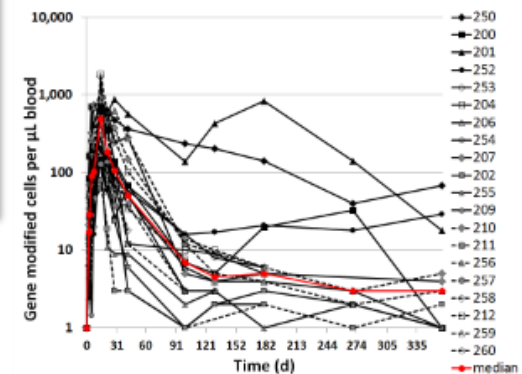
CAR and TCR products associated with long term persistence use this technology; some examples...



*Scholler*



*Tebas*



*Rapoport*  
(Adaptimmune data)



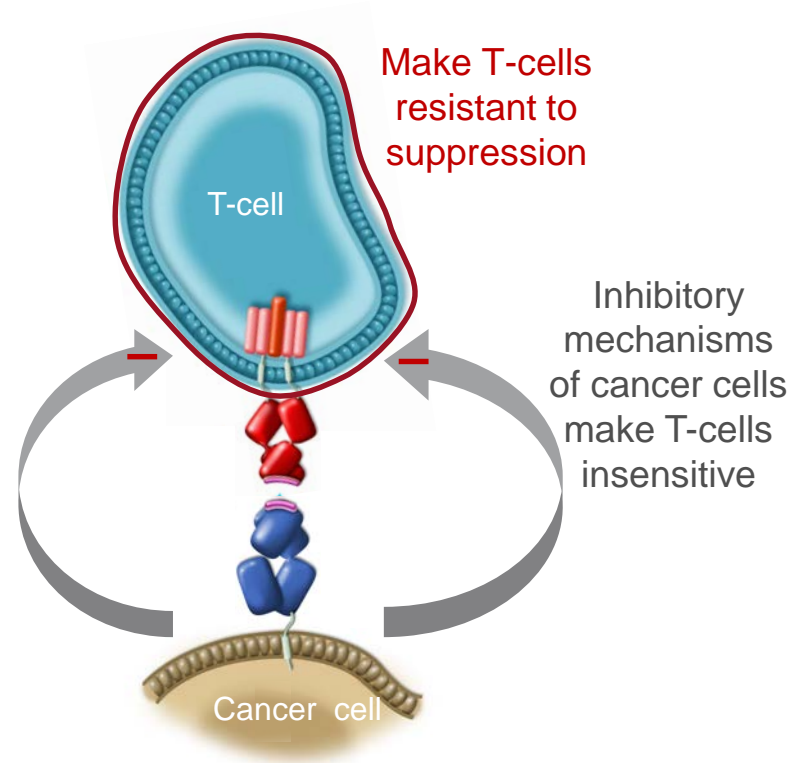
## THE NEXT GENERATION OF SPEAR T-CELLS

# ADOPTIVE T-CELL

## GENERATION 2

Four components to an effective adoptive therapy:

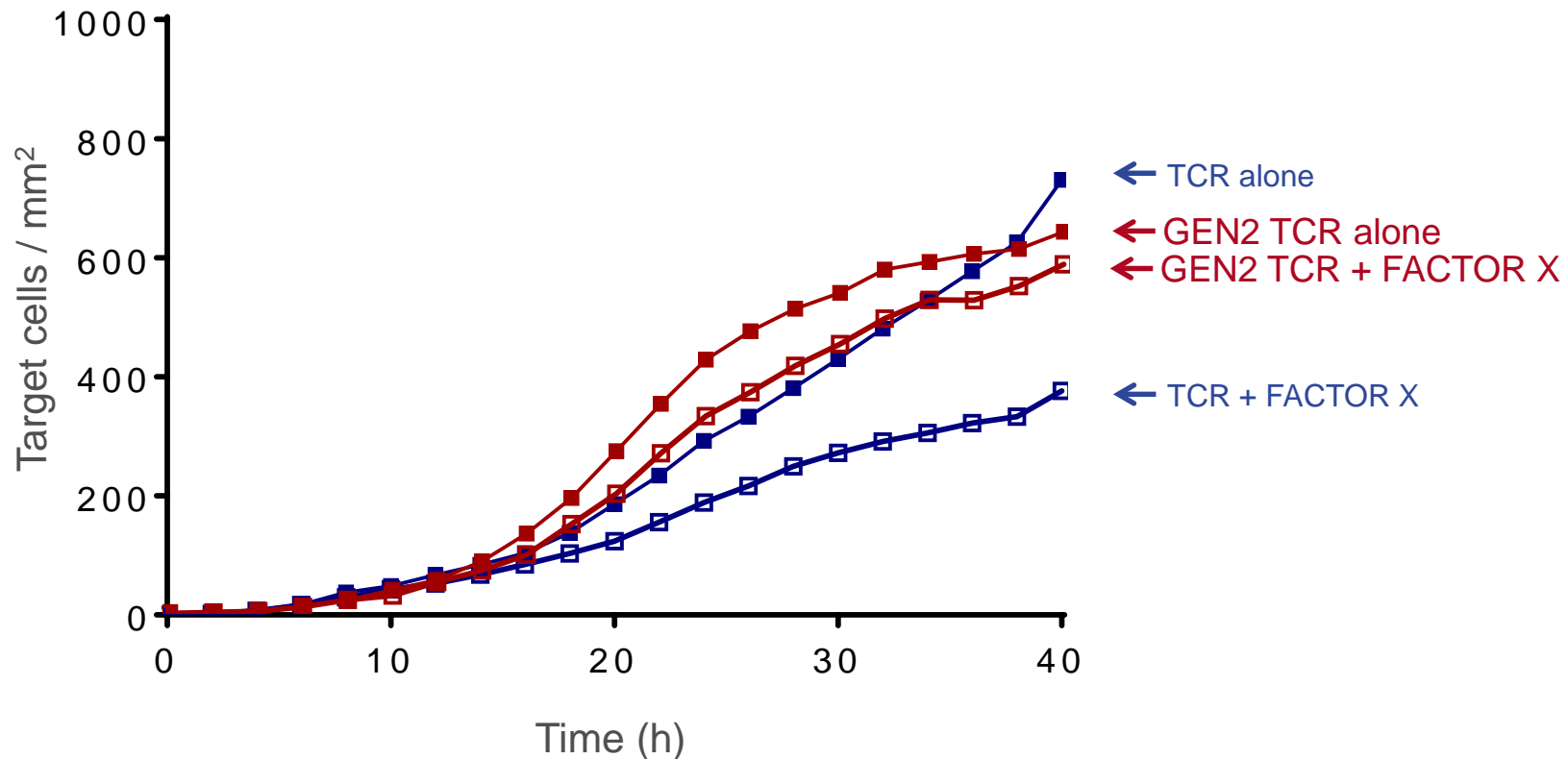
1. T-cell must recognize a cancer cell via a **guiding receptor**
2. The guiding receptor must have two important aspects
  - ♦ Affinity
  - ♦ Specificity
3. The T-cell needs to be **resistant to suppression**



# OVERCOMING INHIBITION IN THE TUMOR MICROENVIRONMENT

## GEN2(A) MAKES T-CELLS INSENSITIVE TO INHIBITORY FACTOR X

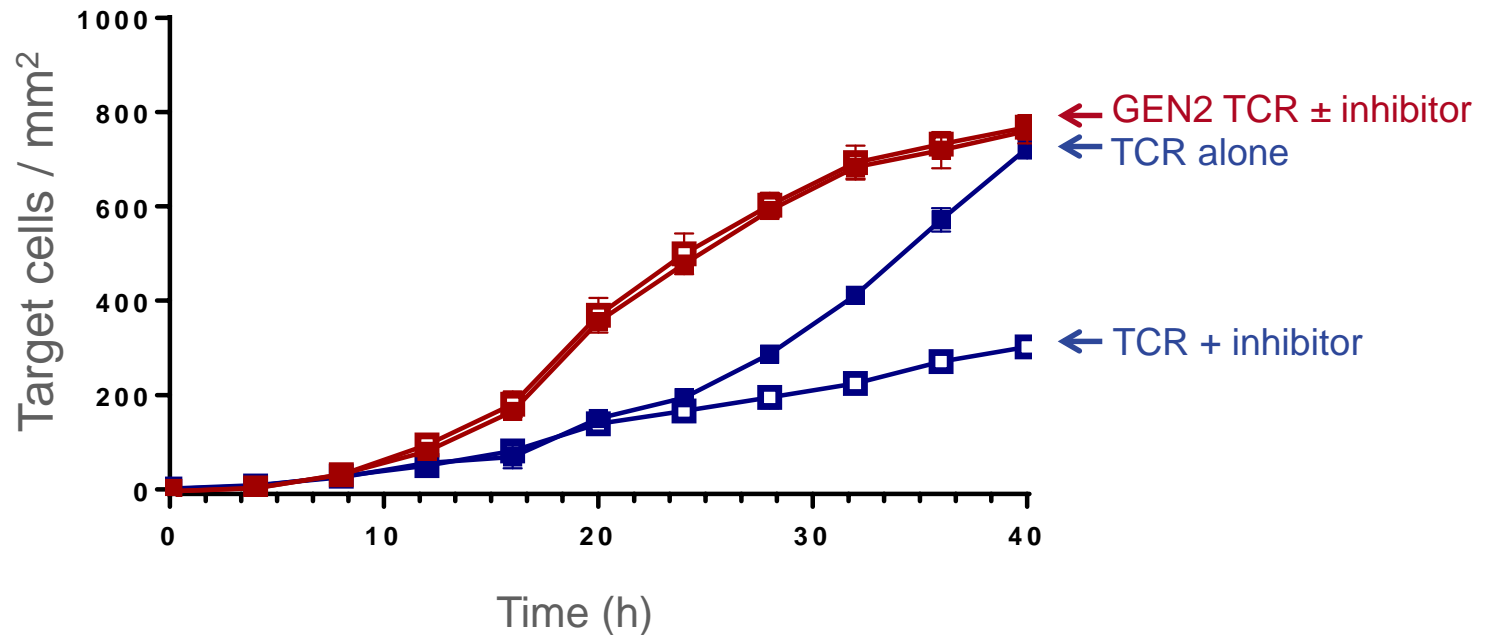
- Gen2(A) TCR maintains enhanced killing in the presence of inhibitors



## OVERCOMING INHIBITION IN THE TUMOR MICROENVIRONMENT (II)

### GEN2(C) MAKES T-CELLS INSENSITIVE TO INHIBITORY FACTORS Y & Z

- Gen2(C) TCR maintains enhanced killing in the presence of inhibitors







## 2016 MILESTONES



## 2016 MILESTONES

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- MAGE-A10 SPEAR T-cell IND open
  - Six US centers now screening
- AFP SPEAR T-cell IND open
  - Centers due to start screening at year-end
- Manufacturing supply agreement signed with Thermo Fisher
- MAGE-A4 named as next target: IND 2017

## 2016 MILESTONES (CONTINUED)

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- NY-ESO SPEAR T-cell
  - Breakthrough status achieved (US)
  - Orphan drug status achieved (US)
  - Positive opinion for orphan status adopted by COMP (EU)
  - Response seen in low expresser cohort
  - Initial results suggest Fludarabine required for T-cell expansion
  - Esophageal study reopening in Europe
  - ASCO safety data encouraging
  - GSK agreement renegotiated
    - ♦ Sarcoma pivotal studies to start 4Q16/1Q17
    - ♦ Combination study to start 2016
    - ♦ At least one Generation 2 SPEAR T-cell IND in 2017

## ADAPTIMMUNE: LEADING THE TCR T-CELL SPACE

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Clear scientific leadership in the field of T-cell engineering

Most compelling clinical data in the field

Deep pipeline across major cancers

Strong financial position

Proven ability to execute

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**Goal: first TCR T-cell therapy to market**

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