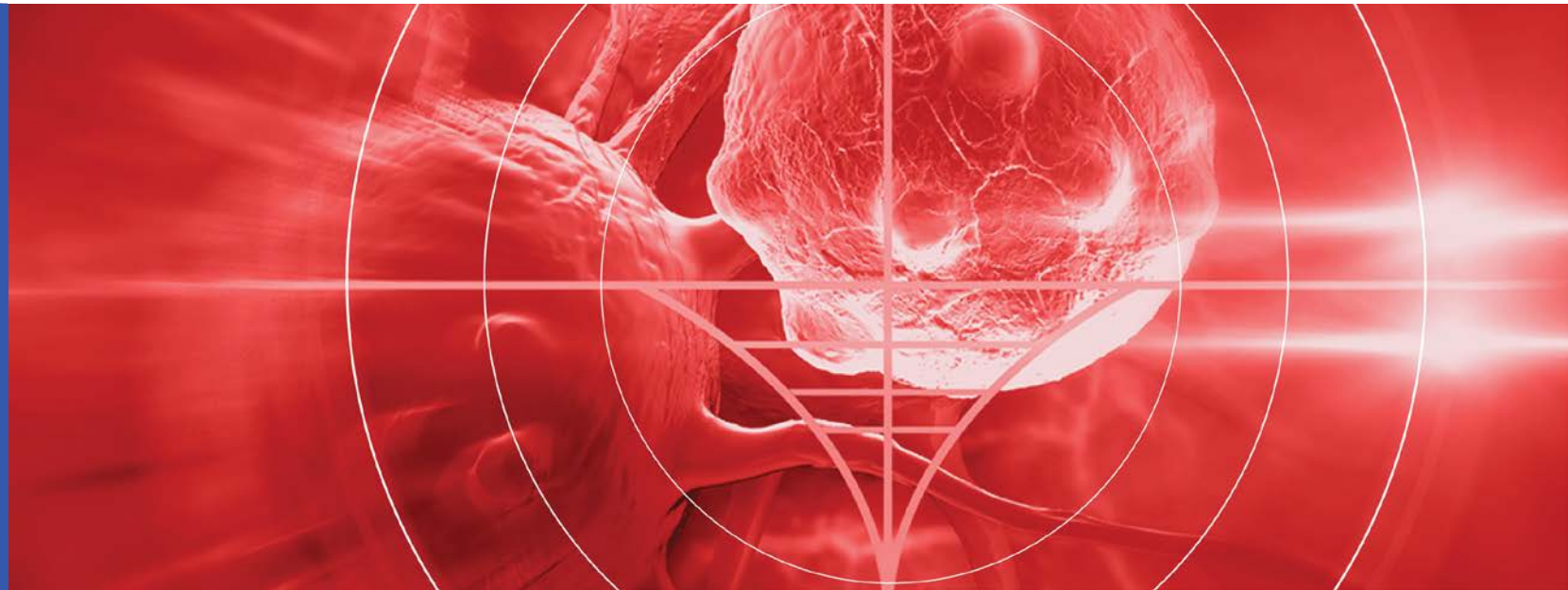
ADAPTIMMUNE INVESTOR PRESENTATION 2016

May 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.

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ADAPTIMMUNE: LEADING THE TCR T-CELL SPACE

- 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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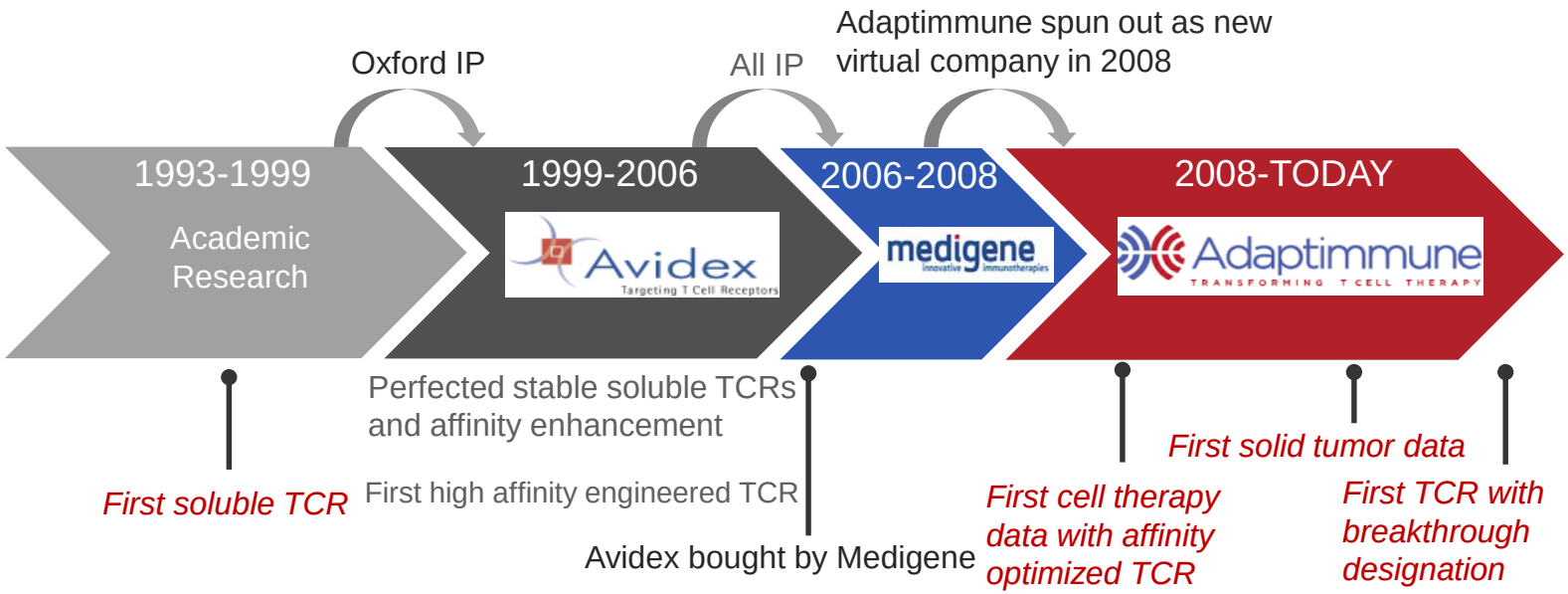
Clear Scientific Leadership

BUILDING A LEADER

A HISTORY OF SCIENTIFIC PRE-EMINENCE

Origins of TCR technology	2005-2007 Collaboration with Steve Rosenberg, MD, Ph.D.	2008-2011 Collaboration with U. Penn	2016 + Adaptimmune SAB



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ADAPTIMMUNE SCIENTIFIC ADVISORY BOARD

Crystal Mackall, M.D., *Chair, Adaptimmune Scientific Advisory Board*; Professor of Pediatrics and Medicine; Associate Director of the Stanford Cancer Institute

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Mario Sznol, M.D., Professor, Internal Medicine; Leader, Disease-Related Research Team, Melanoma and Renal cell Carcinoma; Vice-Chief, Medical Oncology; Co-Director, Yale Skin SPORE, Yale Cancer Center

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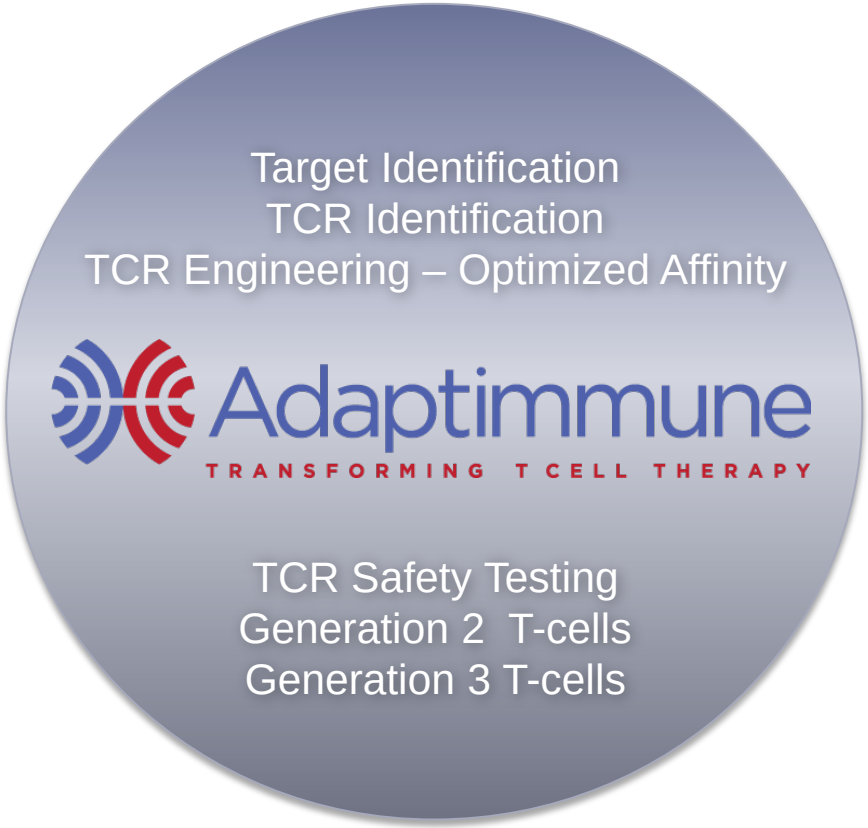
ADAPTIMMUNE SPEAR™ T-CELL PLATFORM



SPEAR
T-CELLS

Specific
Peptide
Enhanced
Affinity
Receptor

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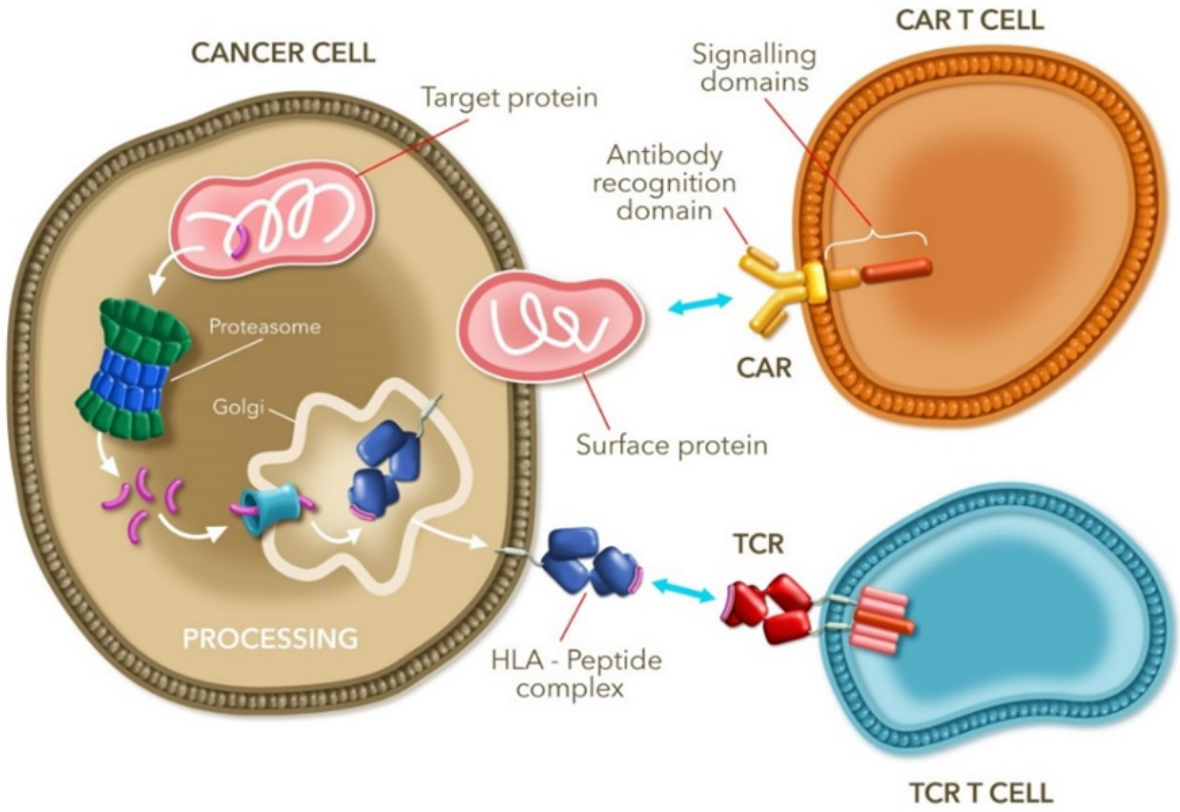
THE SPEAR T-CELL TARGET IS THE HLA-PEPTIDE ANTIGEN

SYNTHETIC RECEPTORS (CAR) AND T-CELL RECEPTORS (TCRs)



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PEPTIDE TARGET VALIDATION VIA MASS SPECTROMETRY

- 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

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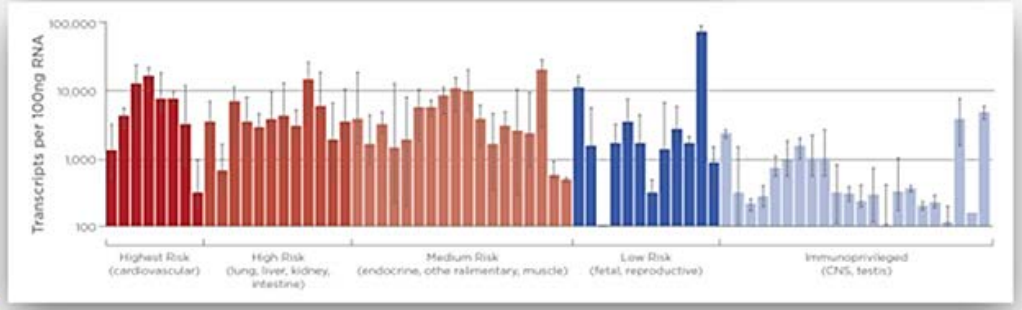
FINDING THE RIGHT TARGETS

Validated Targets → Engineered TCRs → Safety Testing → Robust Manufacturing

Mass spectrometry

Confirms surface expression and expression on tumor cells (i.e. not normal tissue)

INDICATION	FREQUENCY
PROSTATE	100% (inc. androgen independent)
RENAL	90%
LUNG	88%
BLADDER	85%
BREAST	83%



Only **low risk targets** selected for TCR programs

Over thirty validated targets and growing

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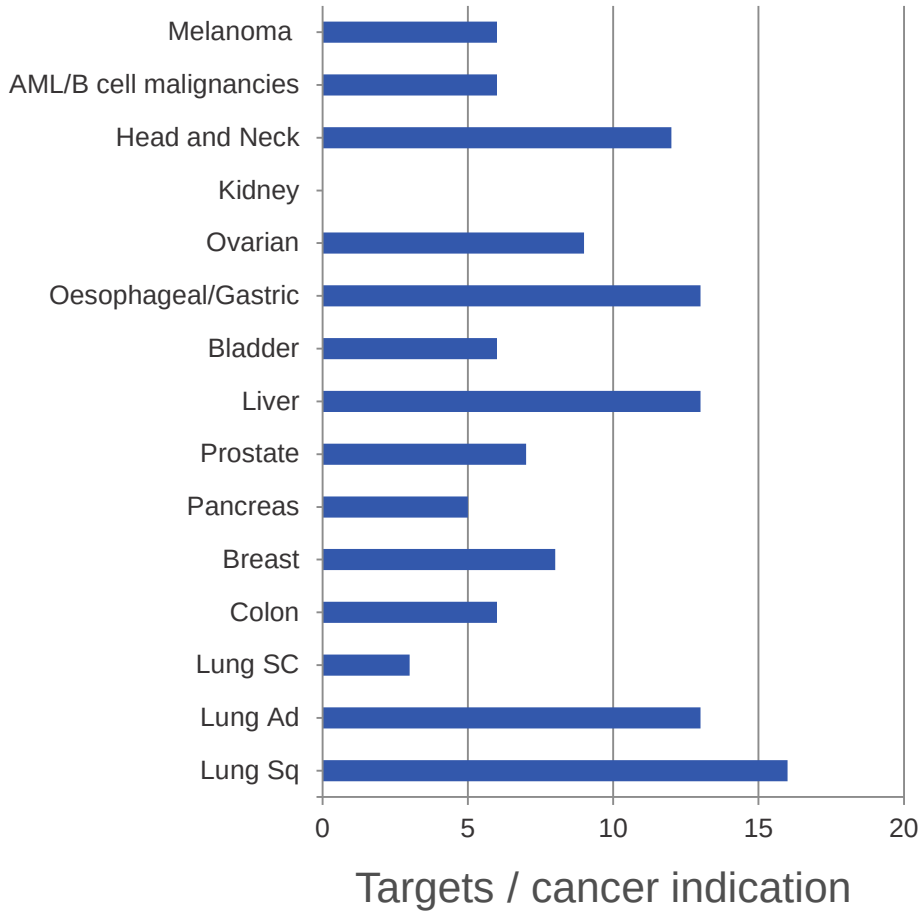
RECENTLY FILED PATENTS ON OVER 60 TARGETS



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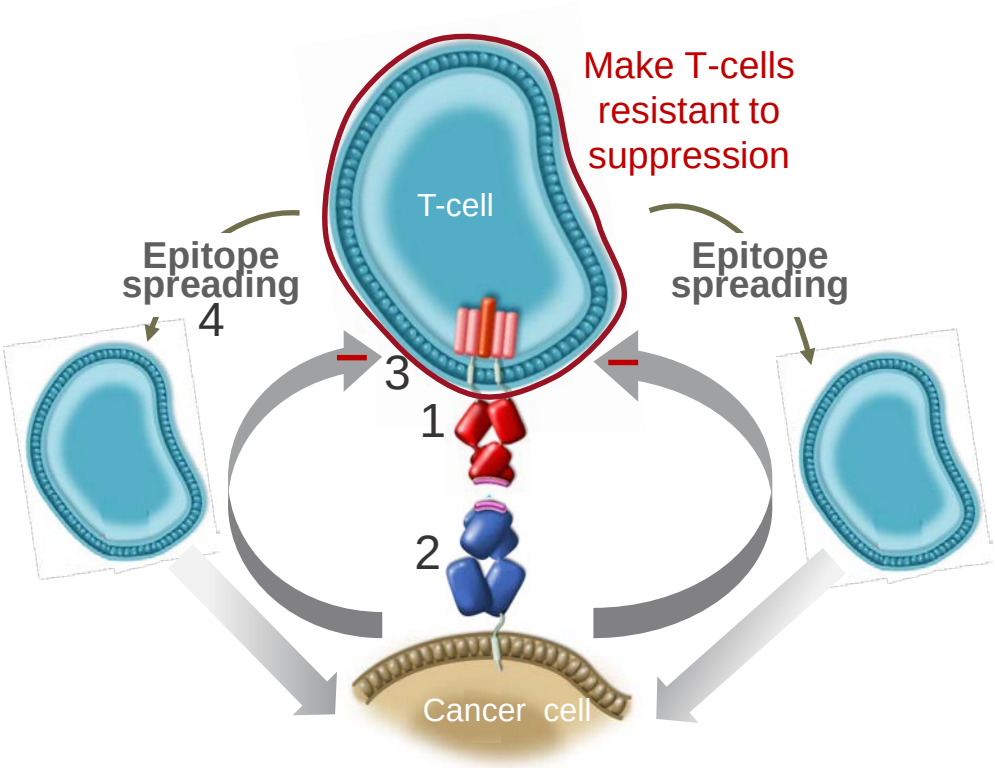
ADOPTIVE T-CELL

MOST POWERFUL UNIT IN IMMUNOTHERAPY

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**
4. The T-cell (either alone or via other mechanisms) needs to **'break cancer immune tolerance'**



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NATURAL T-CELLS ARE ILL-EQUIPPED TO CLEAR CANCER

- Due to negative selection, virtually all natural T-cells that have self peptide specificity will have low affinity TCRs
  - This mechanism guards the body against autoimmunity
- However, all reasonably prevalent peptide antigens of cancer relevance are of self origin
  - Many of these peptide antigens are derived from proteins for which the encoding gene is silenced (or severely suppressed) in all (or almost all) adult tissues

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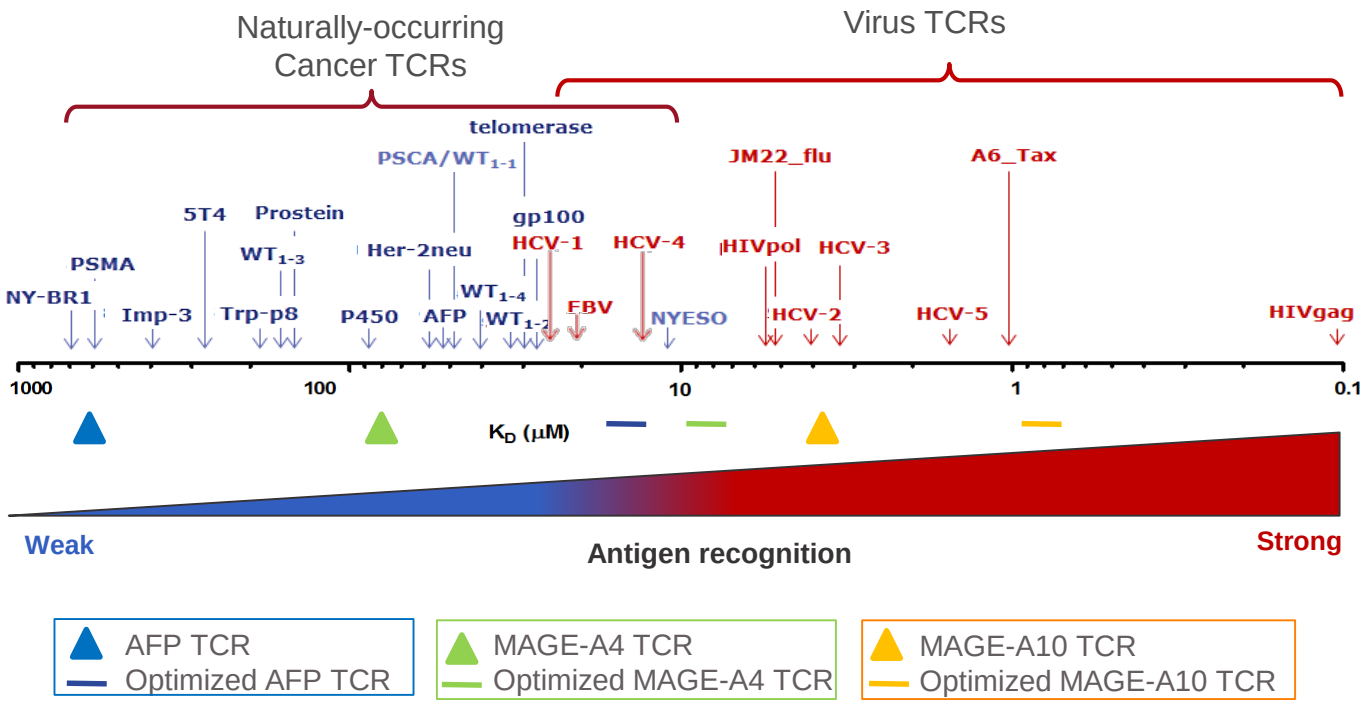
AFFINITY OPTIMIZATION IS IMPORTANT IN ALL CASES SO FAR

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

Aleksic, M. et al. (2012). Eur J Immunol 10.1002/eji.201242606

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AFFINITY OPTIMIZING CANCER TCRs IS VITAL TO T-CELL FUNCTION

- Some non-engineered TCRs will recognise antigen well
  - e.g. NY-ESO
  - Even so, cancer cell killing is dramatically improved by affinity optimization
- Some non-engineered TCRs fail to recognize antigen well
  - e.g. MAGE-A4
  - The optimal affinity is crucial for T-cell function and the same across all cancer cell lines

Affinity engineering is a critical step in TCR optimization

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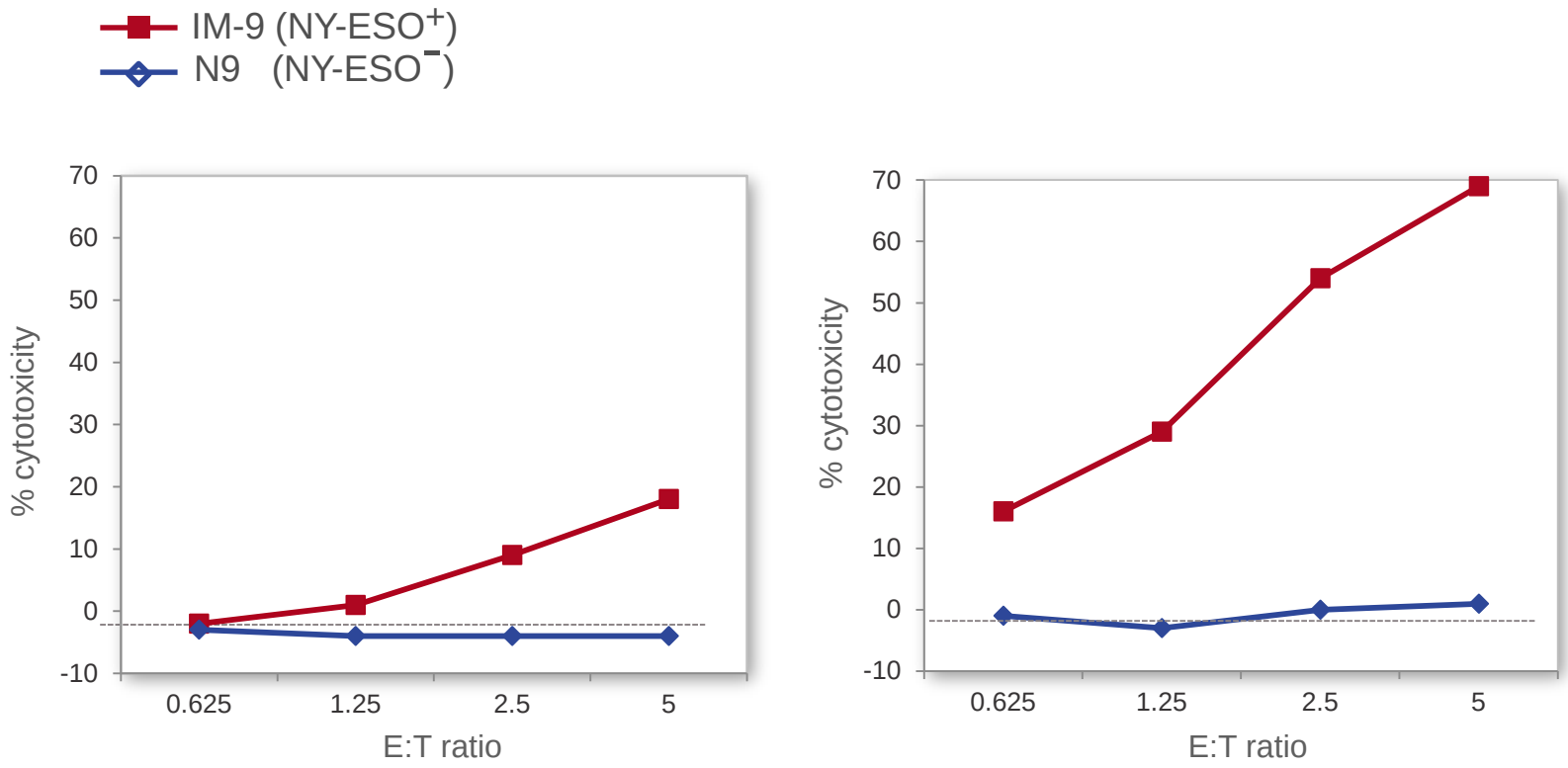
NY-ESO: NATURAL VERSUS ENGINEERED TCR FUNCTIONALITY



Even for NY-ESO, affinity engineering improves cancer killing

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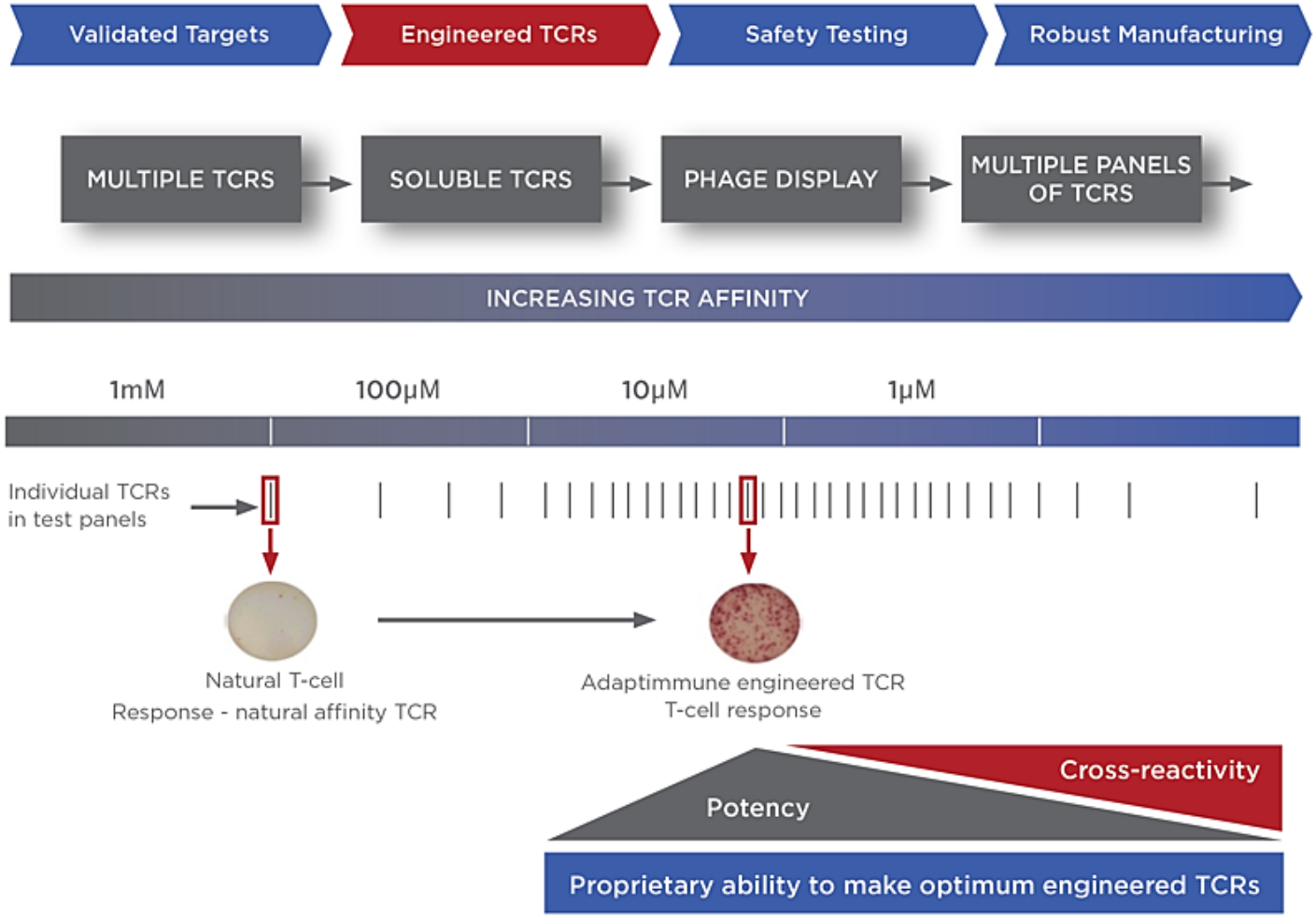
FINDING THE RIGHT TCR AFFINITY



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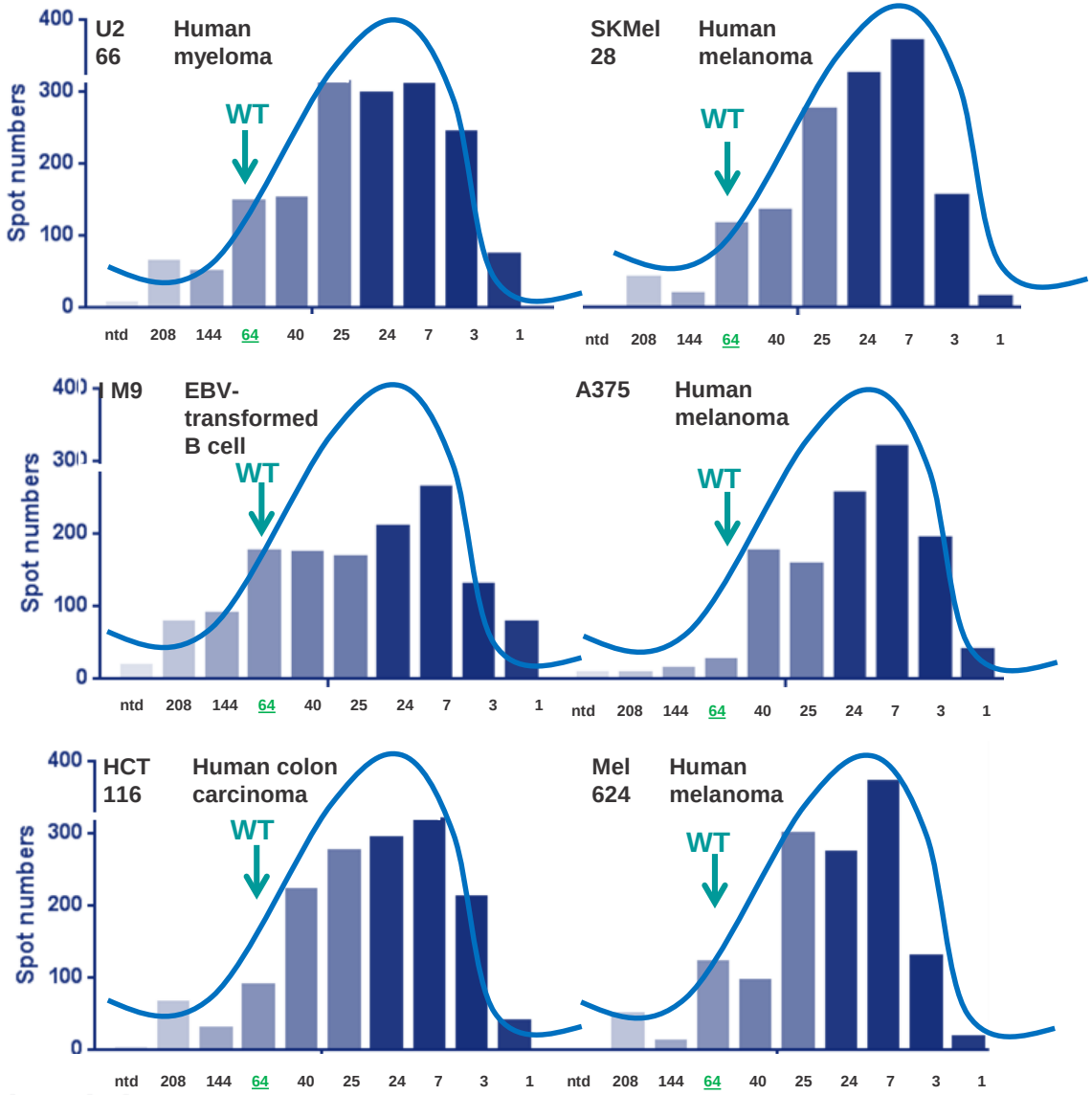
MAGE-A4: EFFECT OF OPTIMIZING TCR AFFINITY



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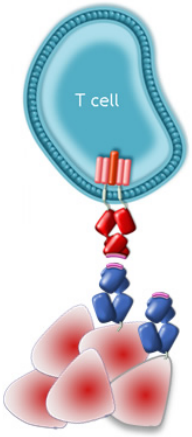
SAFETY - SPECIFICITY AND NON-SPECIFICITY

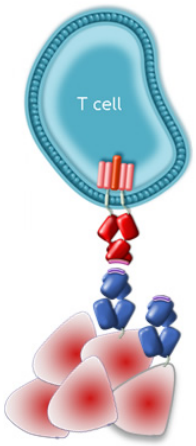
ON TARGET



Target antigen on normal tissue

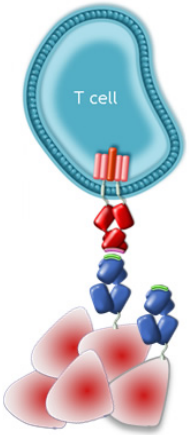
normal tissue

OFF TARGET (SPECIFIC)



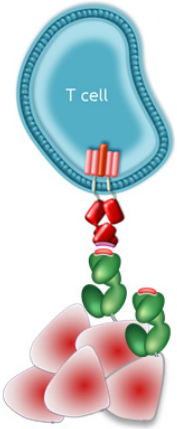
Closely related antigen on normal tissue

OFF TARGET (NON-SPECIFIC)



Promiscuous recognition (unrelated to target)

ALLOREACTIVITY



Alternate HLA restriction

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ADOPTIVE T-CELL

GENERATION 2

Four components to an effective adoptive therapy:

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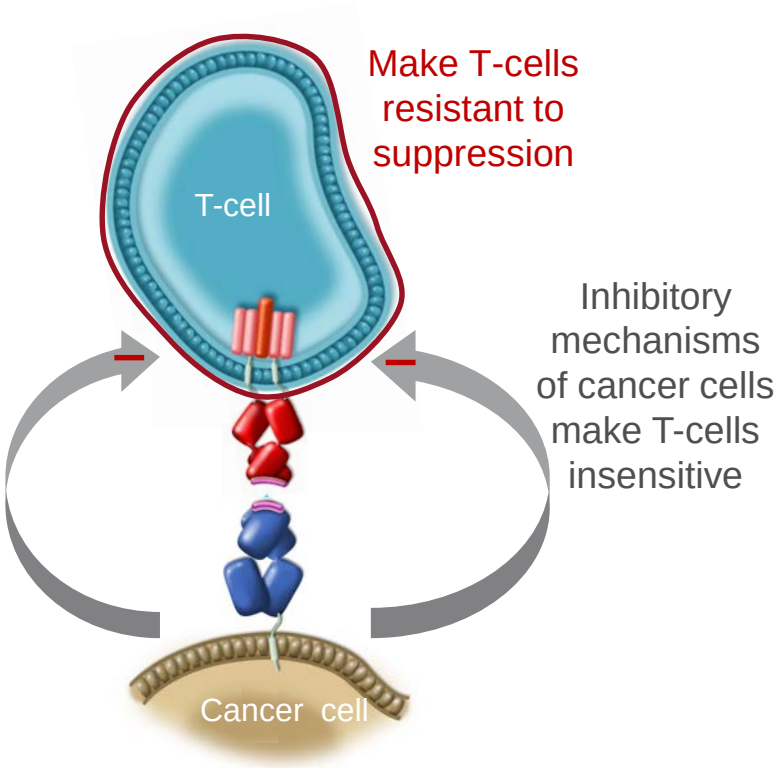
2. The guiding receptor must have two important aspects
   - **Affinity**
   - **Specificity**

3. The T-cell needs to be **resistant to suppression**



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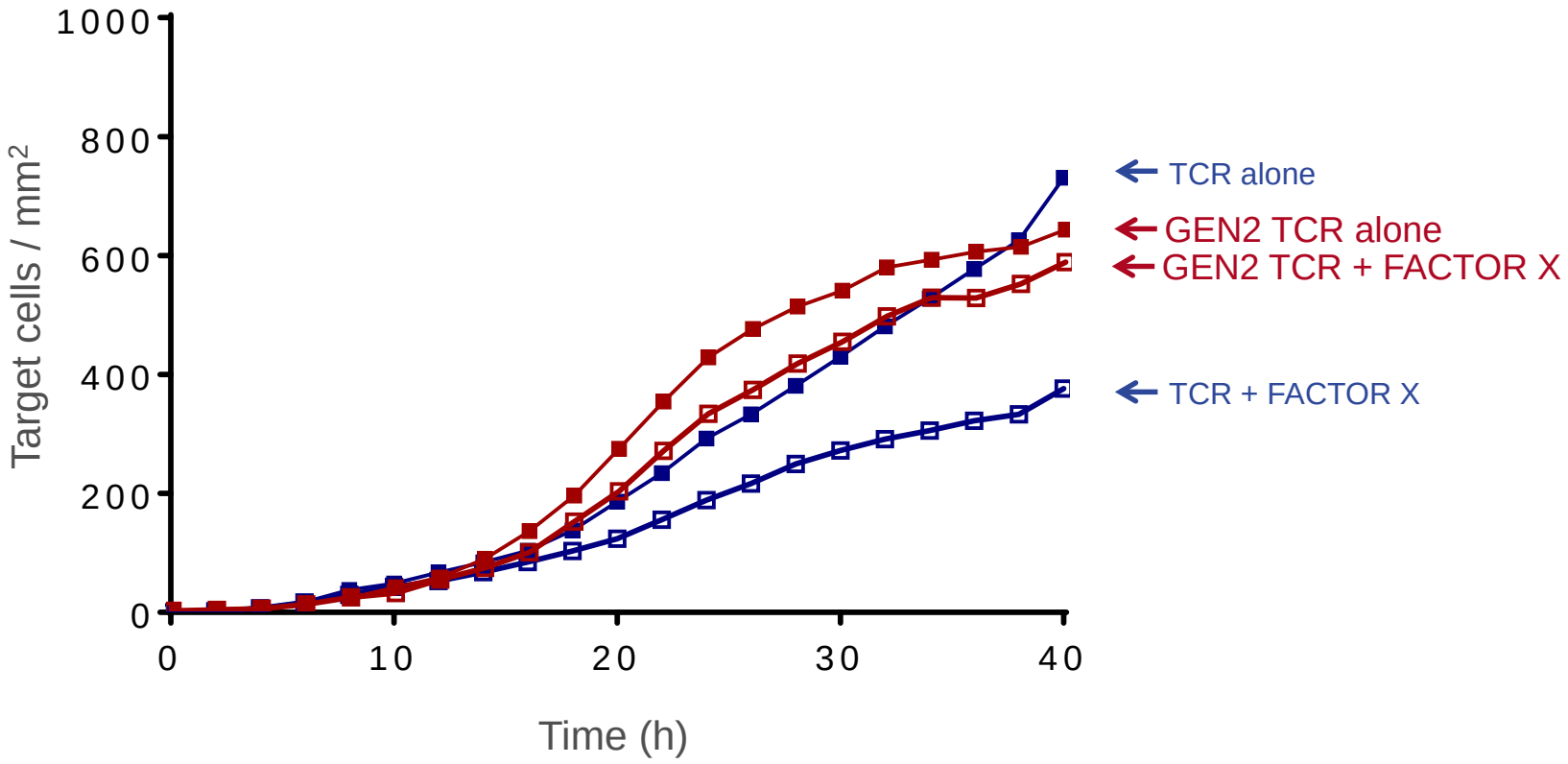
OVERCOMING INHIBITION IN THE TUMOUR MICROENVIRONMENT

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

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



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Clinical Data - Headlines

INDUSTRY-LEADING TCR PIPELINE IN SOLID AND HEMATOLOGIC CANCERS

ONGOING PROGRAMS FOR NY-ESO SPEAR T-CELL

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

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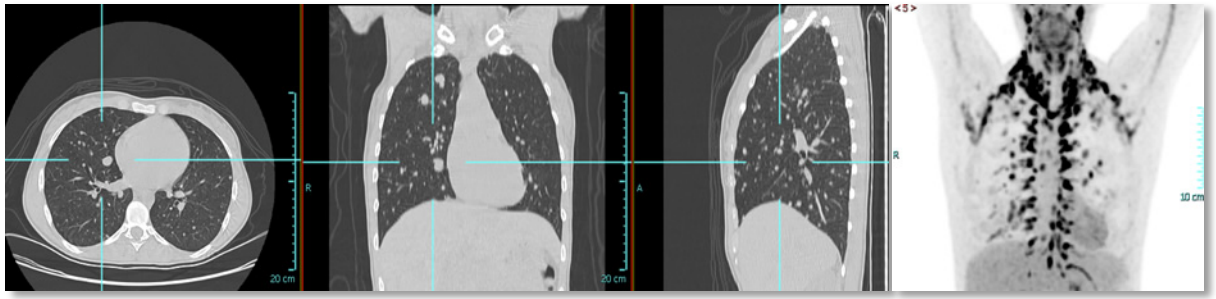
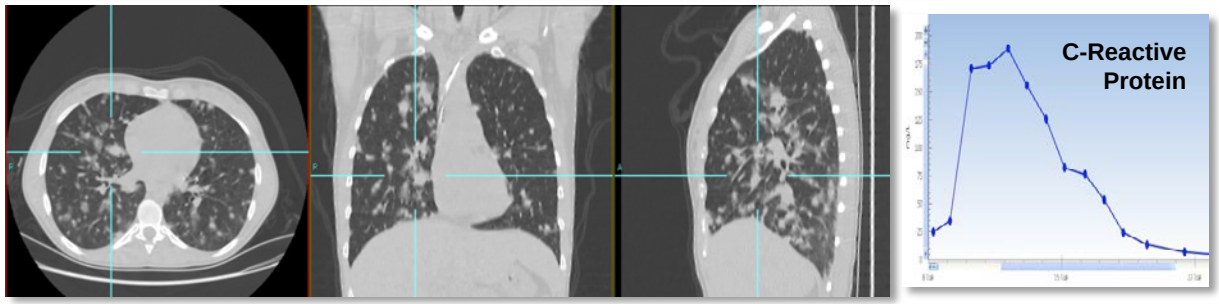
PHASE I/II STUDY IN SYNOVIAL SARCOMA

RADIOGRAPHIC PSEUDOPROGRESSION AND RESPONSE OF LUNG METASTASES LEADING TO COMPLETE RESPONSE

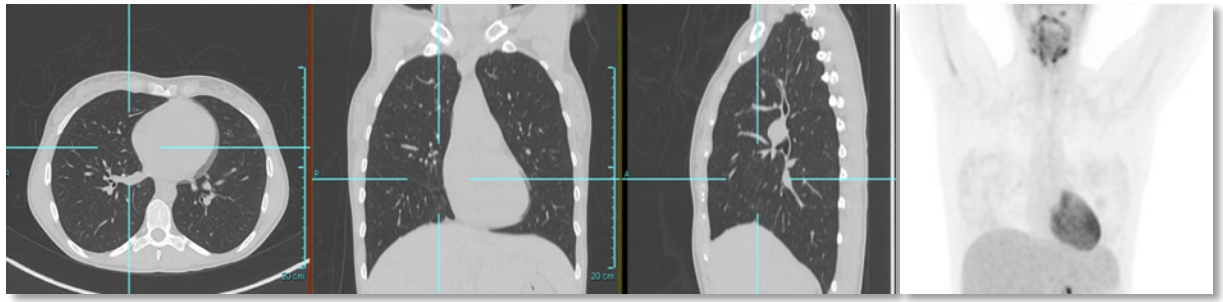
Baseline:
Bilateral miliary metastatic disease



Day +2:
Pseudoprogression due to immune infiltration



Day +101:
Complete Response



Source: AACR April 2015

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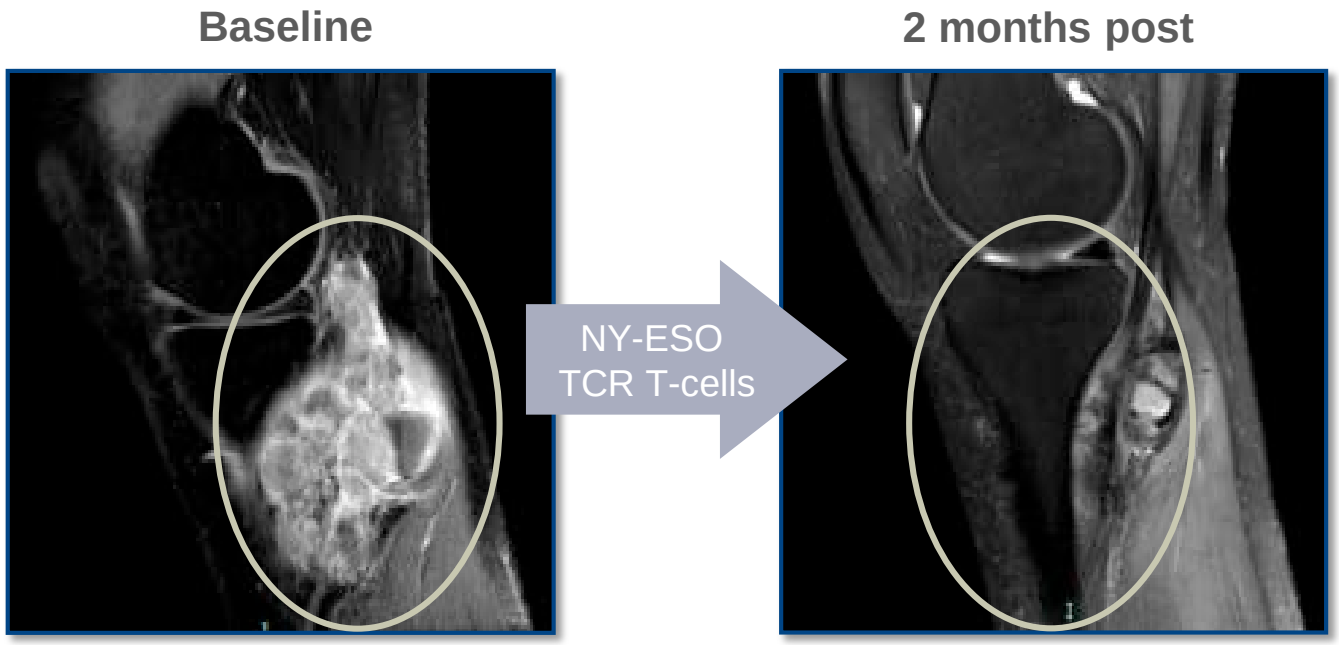
NEAR COMPLETE RESPONSE TO NY-ESO-1 T-CELLS OF UNRESECTABLE PRIMARY TUMOR IN THE KNEE



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

Source: SITC, November 2015

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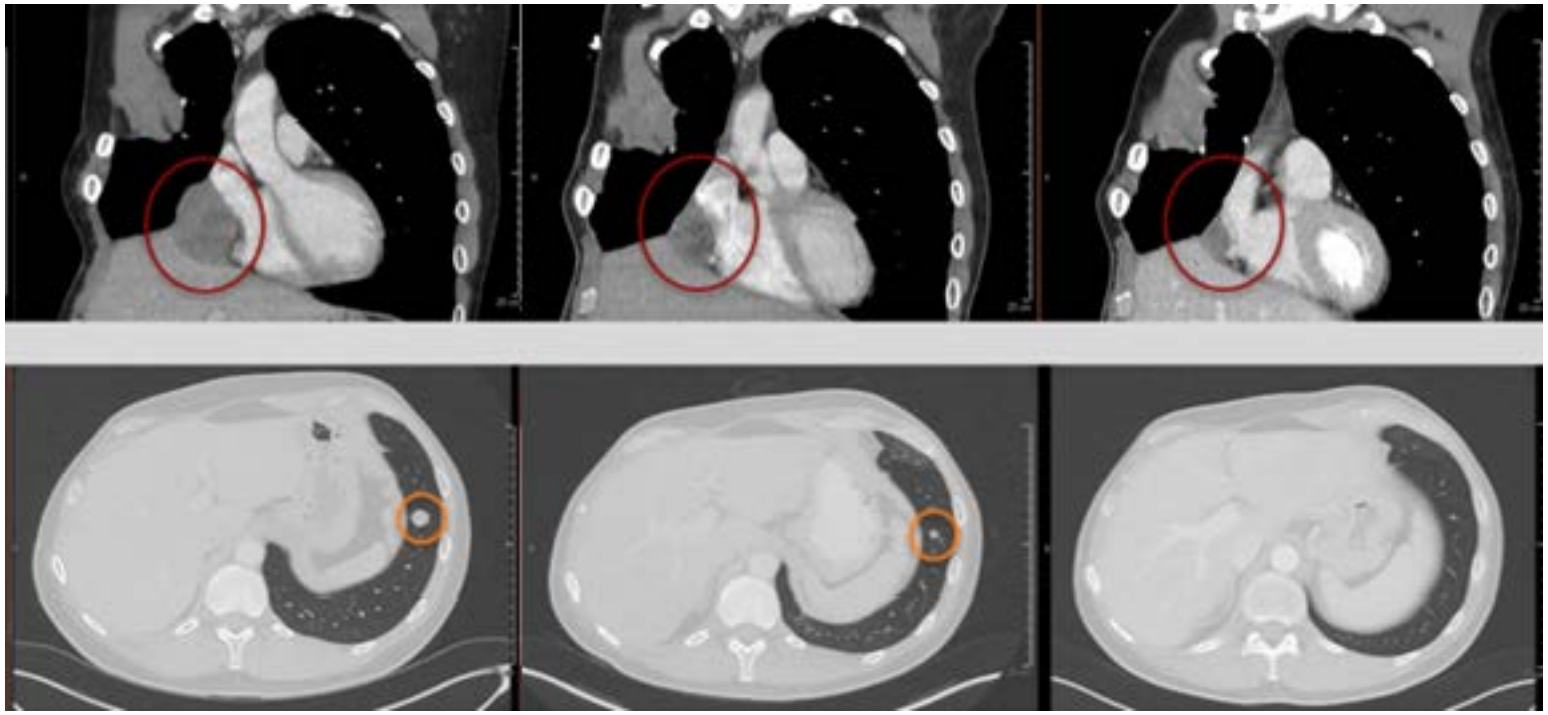
TUMOR SHRINKAGE OVER THE COURSE OF SEVERAL MONTHS FOLLOWING NY-ESO-1 TCR FOR SYNOVIAL SARCOMA

MULTIPLY RECURRENT, UNRESECTABLE PULMONARY MASSES

Baseline | 2 months | 12 months



Ongoing PR 400+ days post T-cell infusion

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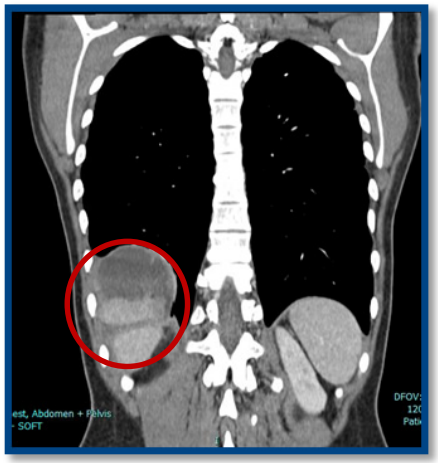
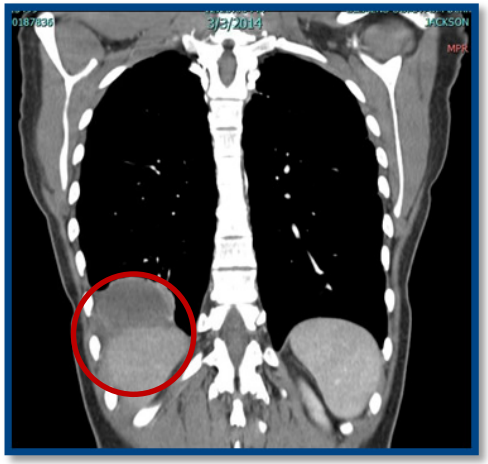
Source: Adaptimmune

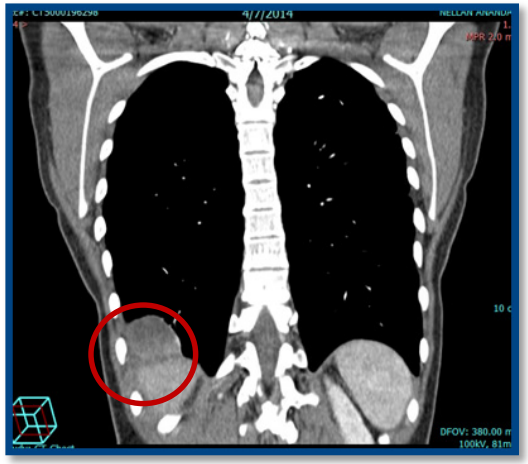
CLINICAL RESPONSE FOLLOWED BY RESECTION AT PROGRESSION



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

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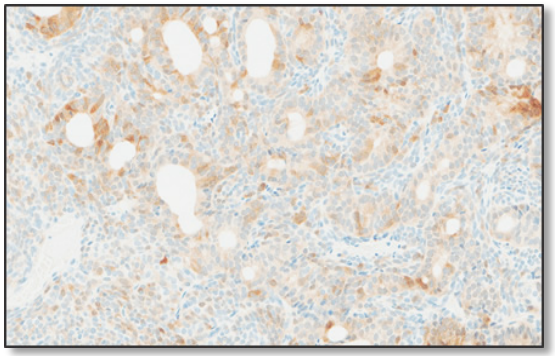
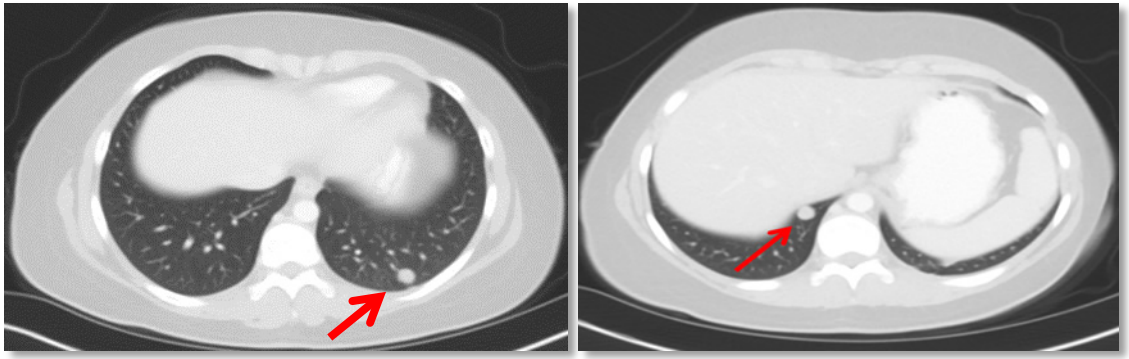
CLINICAL RESPONSES OBSERVED ACROSS A SPECTRUM OF NY-ESO-1 EXPRESSION

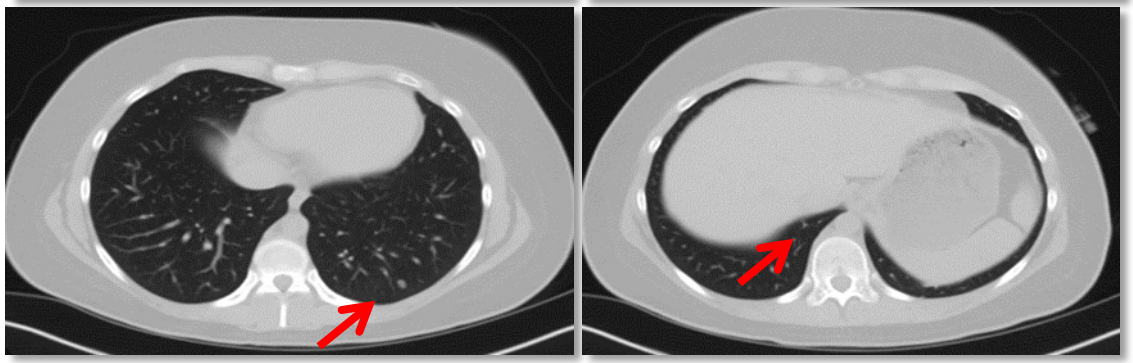
RESPONSE IN A PATIENT WITH LOW NY-ESO-1 EXPRESSION



Baseline
11-05-13



Month 3
02-18-14



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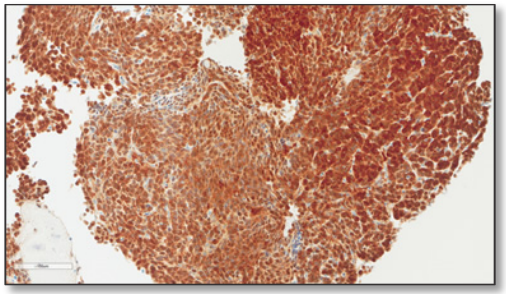
Source: Adaptimmune

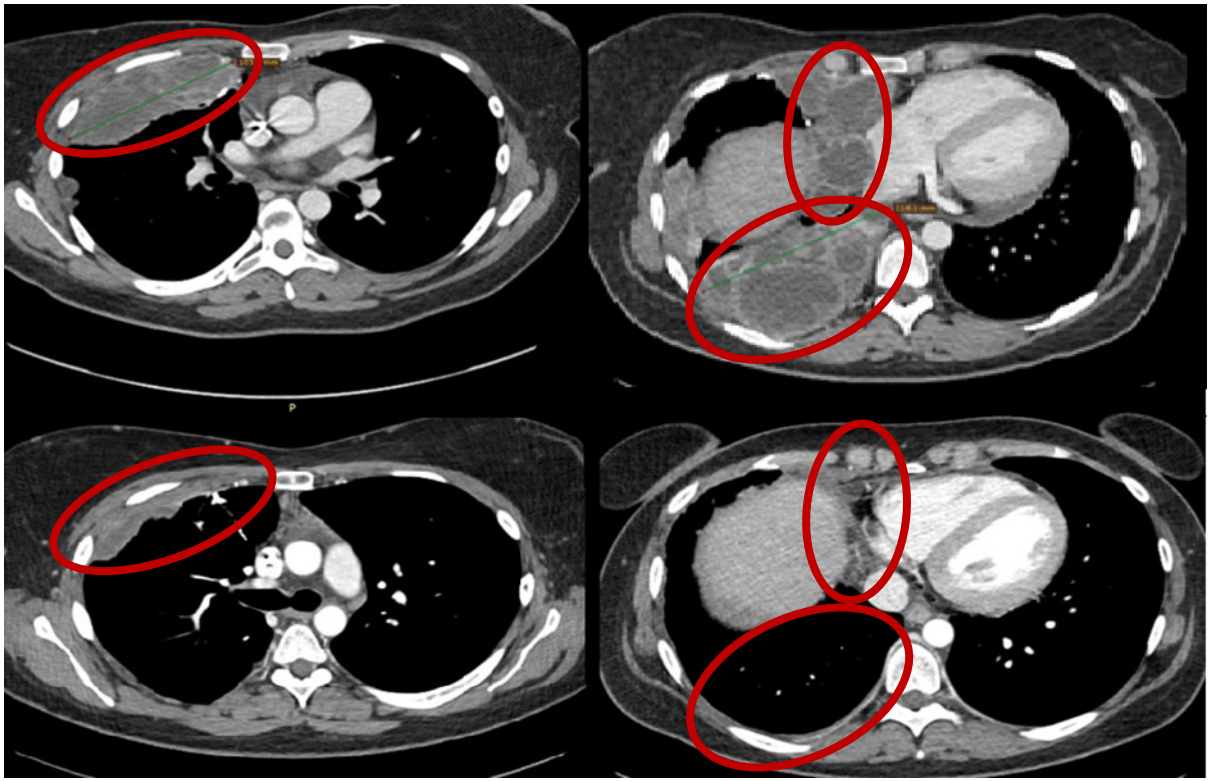
CLINICAL RESPONSES OBSERVED ACROSS A SPECTRUM OF NY-ESO-1 EXPRESSION

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



Baseline

Month 6



Source: Adaptimmune

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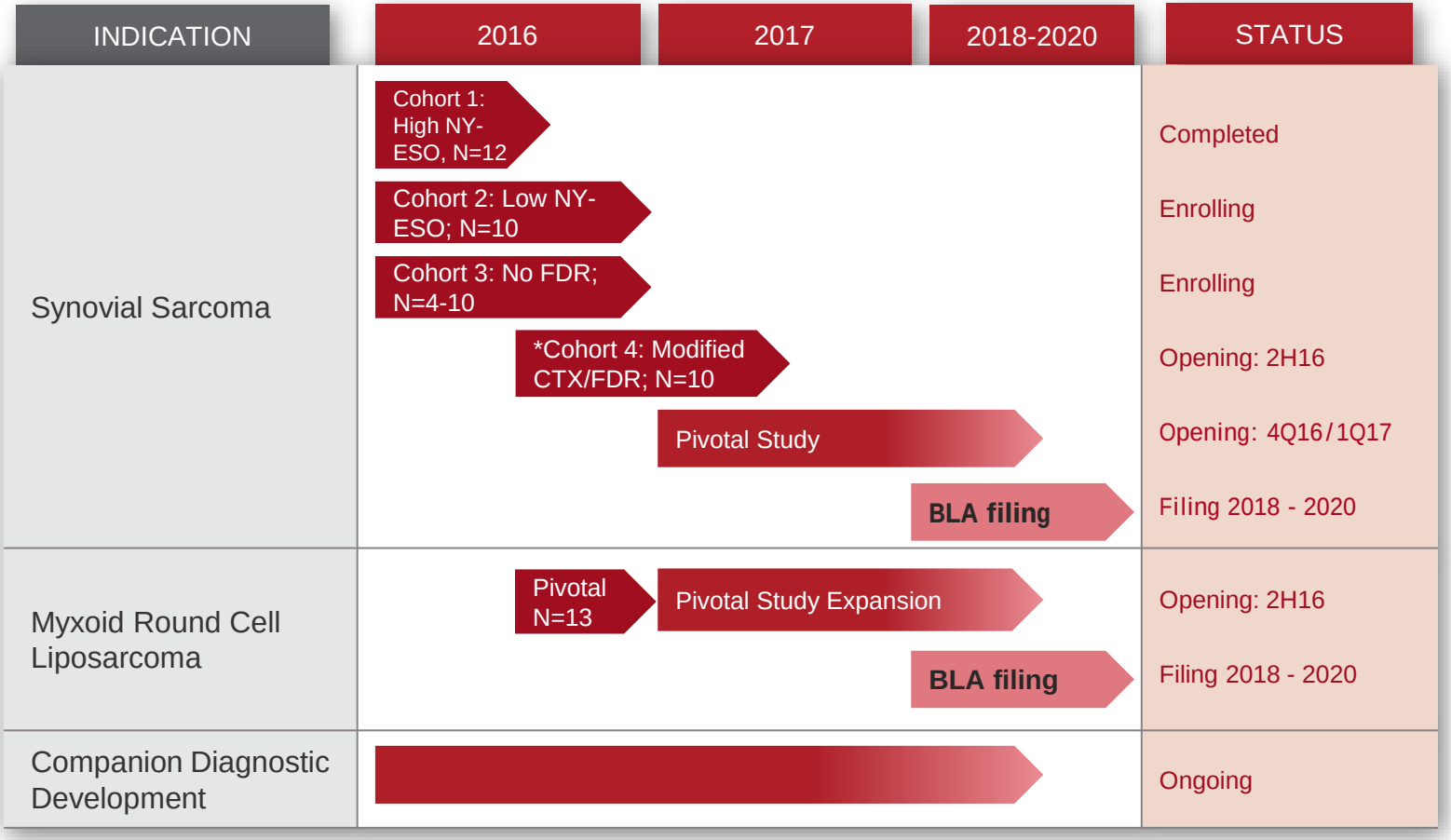
NY-ESO CLINICAL PROGRAM: REGISTRATION PLAN IN SARCOMA

BREAKTHROUGH & ORPHAN DESIGNATION GRANTED



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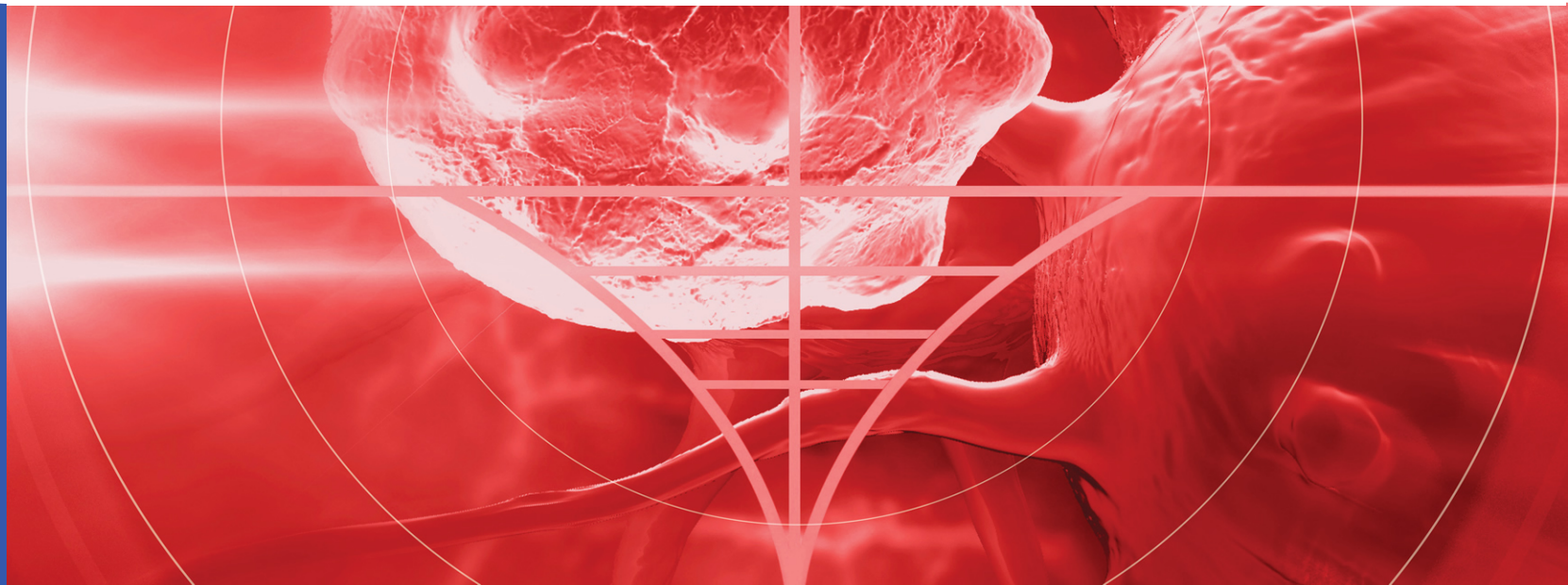
Proprietary Pipeline



CLINICAL PROGRAM UPDATE

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 TCR			RAC and IND submission in 2017
Multiple cancer types	Generation 2 and 3 TCRs			INDs in 2017+
Multiple cancer types	Undisclosed			INDs from 2017+

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CANCER TESTIS EXPRESSION

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%

Source: TGCA RNAseq datasets

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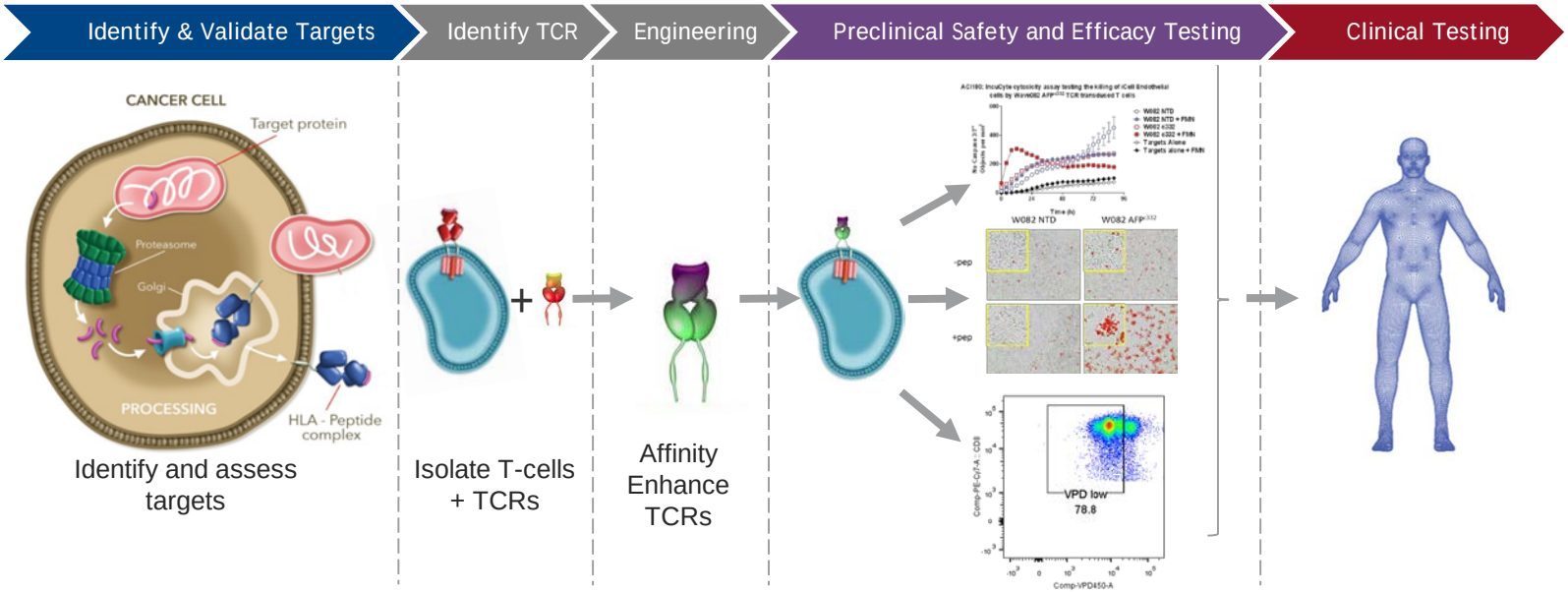
THE PIPELINE ENGINE



- SPEAR T-cell platform supports development across different HLA types
- 3 HLA types cover ~70% of the world population*

* www.allelefrequencies.net; internal model

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WHOLLY OWNED TARGET PIPELINE (APRIL 2016)

Cancer indication	Top 3 Targets Identified for Each Indication (%) TCGA		
	Target 1	Target 2	Target 3
Sarcoma	(30%)	(21%)	(17%)
Endometrial	(27%)	(23%)	
Esophageal	(72%)	(40%)	(38%)
Lymphoid neoplasm	(29%)	(25%)	(25%)
Gastric	(51%)	(48%)	(45%)
Uveal melanoma	(100%)	(100%)	(100%)
Prostate	(100%)	(99%)	(90-95%)
Pancreatic	(54%)	(49%)	(37%)
Ovarian	(54%)		
Lung AD	(43%)	(34%)	(34%)
Lung SqCC	(58%)	(47%)	(46%)
Liver HCC	(44%)	(36%)	(34%)
Head and Neck SCC	(44%)	(40%)	(38%)
Skin Cutaneous Melanoma	(88%)	(87%)	
Colon	(55%)	(32%)	
Breast	(63%)	(41%)	(25%)
Bladder	(50%)	(41%)	(40%)
AML	(73%)	(50%)	

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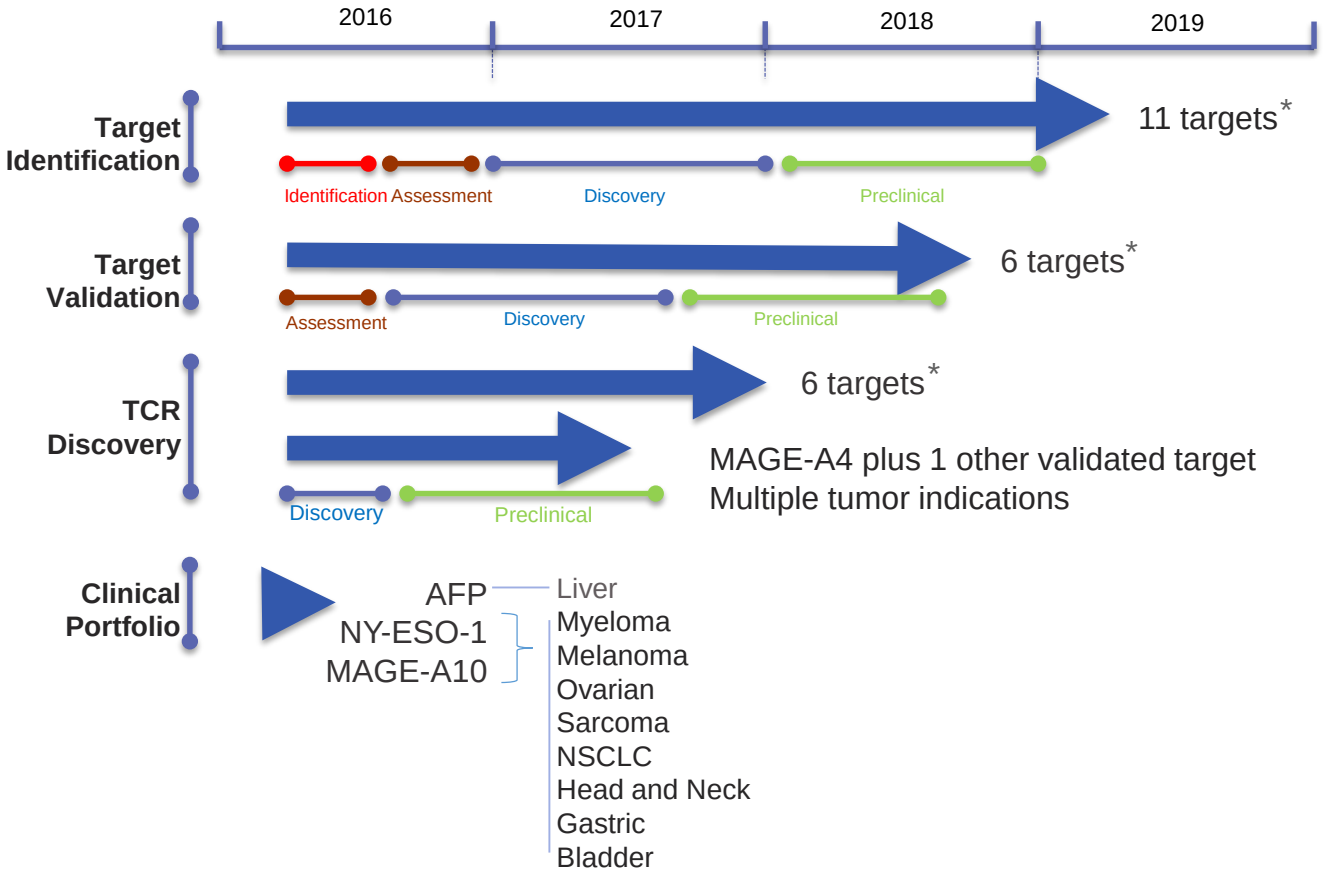
Targets in assessment
New targets due assessment (peptides identified)
Targets with TCRs in the discovery/optimization program
BLUE Cancer Testis Antigens

MULTIPLE TARGETS TO ENTER CLINIC IN NEXT 3 YEARS

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

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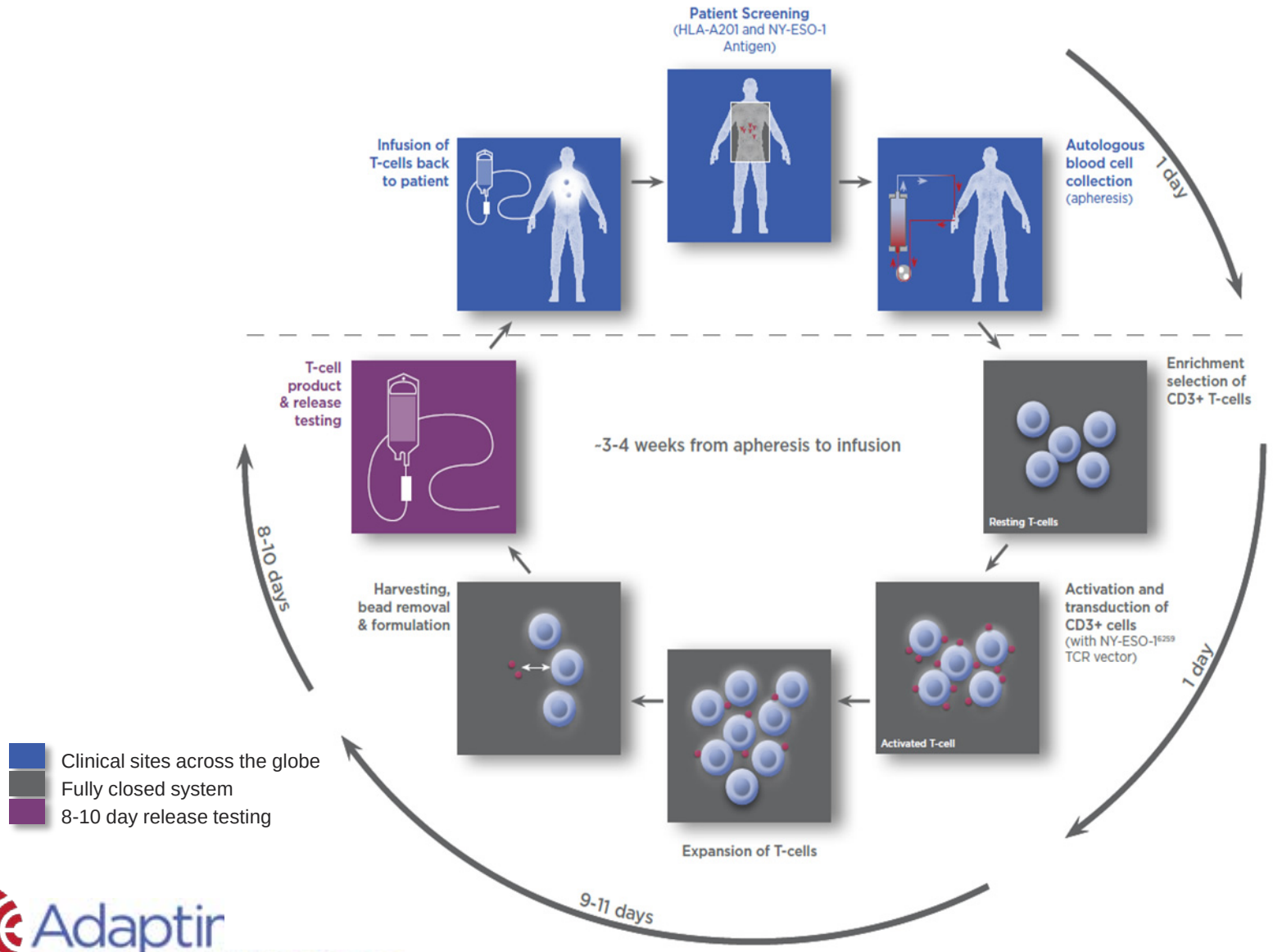
* Early targets – attrition expected

Manufacturing Excellence and Commercial Delivery

MANUFACTURING PROCESS OVERVIEW



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CONTINUUM OF MANUFACTURING PROCESS DEVELOPMENT

OPTIMIZED FOR COMMERCIAL USE AND OPENING A COMMERCIAL FACILITY

		Adaptimmune process	Adaptimmune process	Commercial ready process
Cell	Commercial expansion method	√	√	√
	Fully closed system		√	√
	Industry standard Good Manufacturing Practices		√	√
	Contract manufacturer – fully controlled and owned process		√	√
	Freeze both ends			√
	Wholly owned facility			√
	Automation of some process steps			√
	Automation of most / all process steps			
Vector	Academic vector backbone	√	√	
	Academic vector production – fixed scale	√	√	
	Proprietary vector backbone			√
	Proprietary vector production - fixed scale			√
	Fully scalable vector production			
		2006	***2013***	***2016 - 2017***

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CONTINUUM OF MANUFACTURING PROCESS DEVELOPMENT

OPTIMIZED FOR COMMERCIAL USE AND OPENING A COMMERCIAL FACILITY

		Adaptimmune process	Adaptimmune process	Commercial ready process	Next generation process
Cell	Commercial expansion method	√	√	√	√
	Fully closed system		√	√	√
	Industry standard Good Manufacturing Practices		√	√	√
	Contract manufacturer – fully controlled and owned process		√	√	√
	Freeze both ends			√	√
	Wholly owned facility			√	√
	Automation of some process steps			√	√
	Automation of most / all process steps				√
Vector	Academic vector backbone	√	√		√
	Academic vector production – fixed scale	√	√		√
	Proprietary vector backbone			√	√
	Proprietary vector production - fixed scale			√	√
	Fully scalable vector production				√
		2006	***2013***	***2016 - 2017***	***2018***

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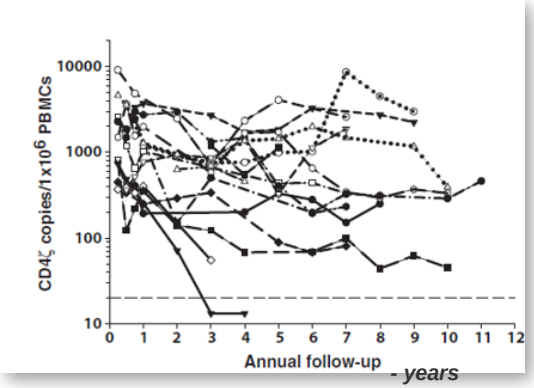
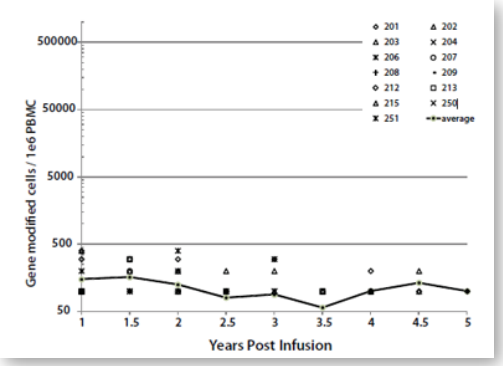
MANUFACTURING THE BEST T-CELLS

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

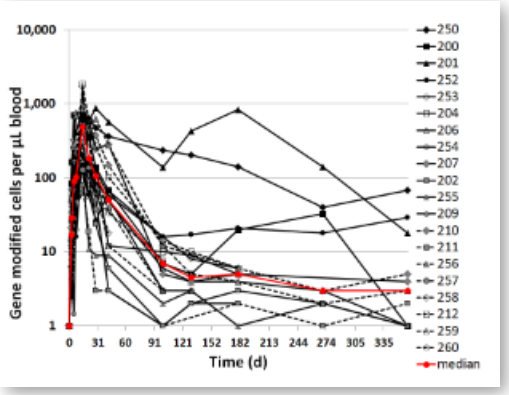
CAR and TCR products associated with long term persistence use this technology; some examples…



Scholler



Tebas



Rapoport
(Adaptimmune data)

Source: Scholler et al, Mol Ther (2013); Tebas et al, Blood (2013); Rapoport et al, Nat Med (2015); Porter et al, STM (2015)

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ADAPTIMMUNE MANUFACTURING SUMMARY

NOT ALL T-CELL MANUFACTURING METHODS ARE EQUAL

- Proprietary T-cell expansion method
  - Produces young, potent, persistent cells
  - Routinely meets required patient doses
- Commercial ready process in place
  - Fully closed
  - No significant changes since initial trials; de-risks regulatory path
- Supply in place
  - US and EU contract manufacturers in place
  - Dedicated manufacturing plant opening 2017

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ADAPTIMMUNE: LEADING THE TCR T-CELL SPACE

Clear scientific leadership in the field of T-cell engineering

- Proprietary SPEAR T-cell technology uniquely delivers:
  - Correctly identified targets
    - Mass spectrometry critical
  - Specificity and optimal affinity
    - Adaptimmune platform finds window of safety and cross reactivity for each TCR
  - "Supra-natural" TCRs to accelerate programs
    - Numerous parental TCRs derived from libraries lead to multiple INDs
  - Enhanced effectiveness of TCRs: Generation 2 and 3
    - Generation 2: Designed to overcome tumor microenvironment
    - Generation 3: Designed to induce epitope spreading and break tumor immune tolerance
- No other company can currently deliver all of these

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ADAPTIMMUNE: LEADING THE TCR T-CELL SPACE

Clear scientific leadership in the field of T-cell engineering

Most compelling clinical data in the field

- Multiple clinical responses in synovial sarcoma, a solid tumor
  - 60% response rate at intended dose
  - Cohort 2 suggests responses in low expressers
  - Cohort 3 suggests importance of fludarabine
  - Cohort 4 starting shortly
- Over 90% response rate in multiple myeloma study in conjunction with ASCT
  - Median overall survival of ~3 years
- No other company is as far advanced as Adaptimmune in the clinic with a TCR T-cell
  - Pivotal studies to start in 4Q16/1Q17

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ADAPTIMMUNE: LEADING THE TCR T-CELL SPACE

Clear scientific leadership in the field of T-cell engineering

Most compelling clinical data in the field

Deep pipeline across major cancers

- Company INDs open for NY-ESO, MAGE-A10 and AFP SPEAR T-cells
  - MAGE-A4 next IND 2017
  - Generation 2 INDs from 2017
- These TCRs all derive from Adaptimmune's proprietary technology
  - Active programs give broad coverage of tumors
- No other company has routinely delivered INDs from in-house TCR platform

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ADAPTIMMUNE: LEADING THE TCR T-CELL SPACE

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

- Total liquidity position of $226 million*
- Current capital can fund the business through mid-2018

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*As of March 31, 2016

ADAPTIMMUNE: LEADING THE TCR T-CELL SPACE

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 (1)

- Milestones met through April 2016
  - Expanded into autoimmune
  - Expanded strategic immunotherapy collaboration with GSK
  - Secured NY-ESO breakthrough therapy designation in synovial sarcoma
  - Secured NY-ESO orphan drug designation
  - IND opened for AFP in hepatocellular cancer

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ADAPTIMMUNE: LEADING THE TCR T-CELL SPACE

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 (2)

- Manufacturing processes optimized
  - Proprietary T-cell expansion method
  - Commercial-ready process in place
  - EU and US contract manufacturers in place

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ADAPTIMMUNE: LEADING THE TCR T-CELL SPACE

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

Goal: first TCR T-cell therapy to market

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ADAPTIMMUNE INVESTOR PRESENTATION 2016

May 2016

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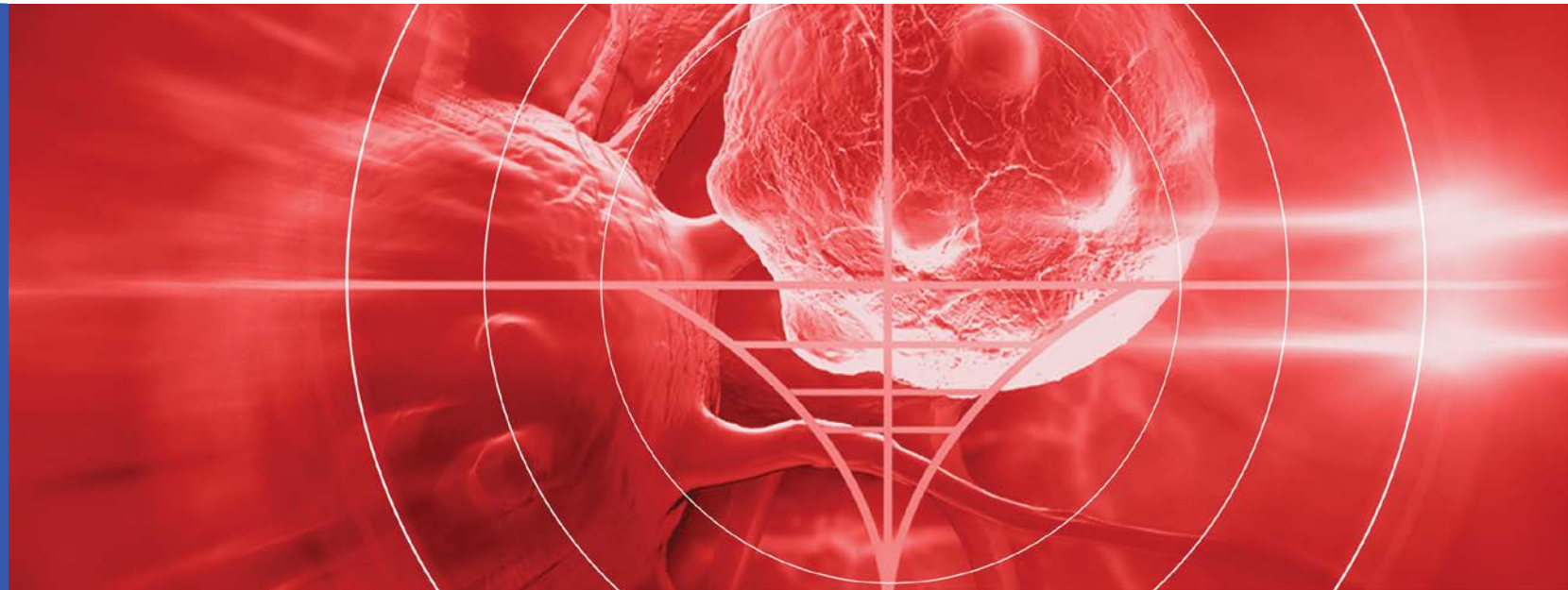
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