

March 2017



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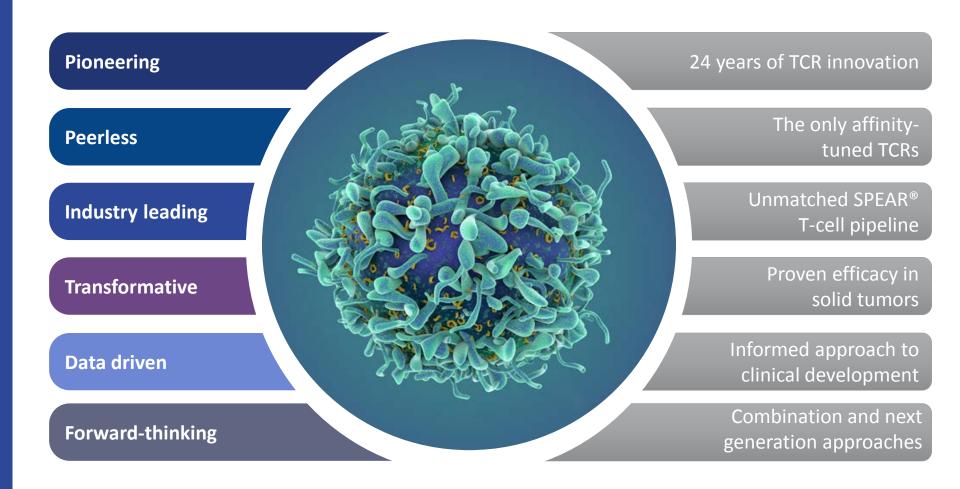
This presentation contains "forward-looking statements," as that term is defined under the Private Securities Litigation Reform Act of 1995 (PSLRA), which statements may be identified by words such as "believe," "may", "will," "estimate," "continue," "anticipate," "intend," "expect" and other words of 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 November 10, 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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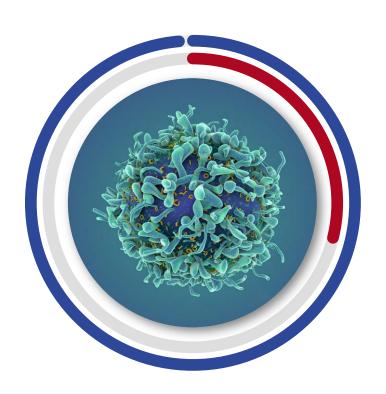
## **Adaptimmune:** Leading the TCR T-cell Space





#### **CAR-T vs TCR:** Differences in Access to Human Proteome

**Significantly Better Access to Peptides with T-cell Receptors** 



Nearly all proteins are available to TCRs

Access to extra- and intracellular proteins

**TCRs** 

Unlimited targets; utilizes the T-cell's native receptor

Affinity tuned SPEAR TCRs overcome low target expression; required to address solid tumors

CAR-T

Only ~28% of proteins available to CAR-T cells

Mostly limited to extracellular proteins

**Limited targets compared to TCRs** 

Chimeric antigen receptor; not designed to recognize an HLA peptide



## Affinity Optimization is Critical to Address Majority of Antigens

Adaptimmune is the Only Company with this Proprietary Technology



- T-cells bind to targets on cancer cells
- Cancer downregulates targets to avoid detection
- Most naturally occurring anti-tumor
   T-cells are low affinity (require more targets)
- SPEAR T-cells are affinity enhanced to overcome this problem
- Proprietary preclinical engineering ensures tumor-specific response
- Optimal specificity and affinity for antitumor activity
- Demonstrated efficacy in solid tumors



### **Developing** Novel TCR Therapies

#### **Utilizing Proprietary Technology Platform to Develop Multiple Approaches**

# Cancer Testis Antigens

- Exclusive to tumor tissue; shown to be good targets
- But expressed less frequently across cancers
- Developing a franchise with overlapping expression profiles
- Examples: NY-ESO,
   MAGE-A10 & -A4

#### **Non-CTA Targets**

- Includes
   oncofetal
   proteins and
   differentiation
   markers
- Closely
   associated with
   single tumor
   types
- Example: AFP

#### **Multiple HLAs**

- Expanding research efforts to target multiple HLAs
- Looking beyond foundational data in HLA-A2

## Next generation SPEAR T-cells

- Data on dnTGF-β receptor construct at SITC 2016
- Also evaluating combination approaches



## **Adaptimmune** Pipeline Overview

#### **Multiple Targets with Near Term Clinical Milestones**



#### **NY-ESO**

- Clinical data in synovial sarcoma and multiple myeloma
- Active trials in synovial sarcoma, MRCLS, ovarian and non-small cell lung cancer (NSCLC)
- Registration studies in synovial sarcoma planned for 2017



#### MAGE-A10

- IND open
- Studies enrolling in head & neck, melanoma, urothelial (bladder), and NSCLC

#### **AFP**

- IND open
- Study in hepatocellular cancer in 2017

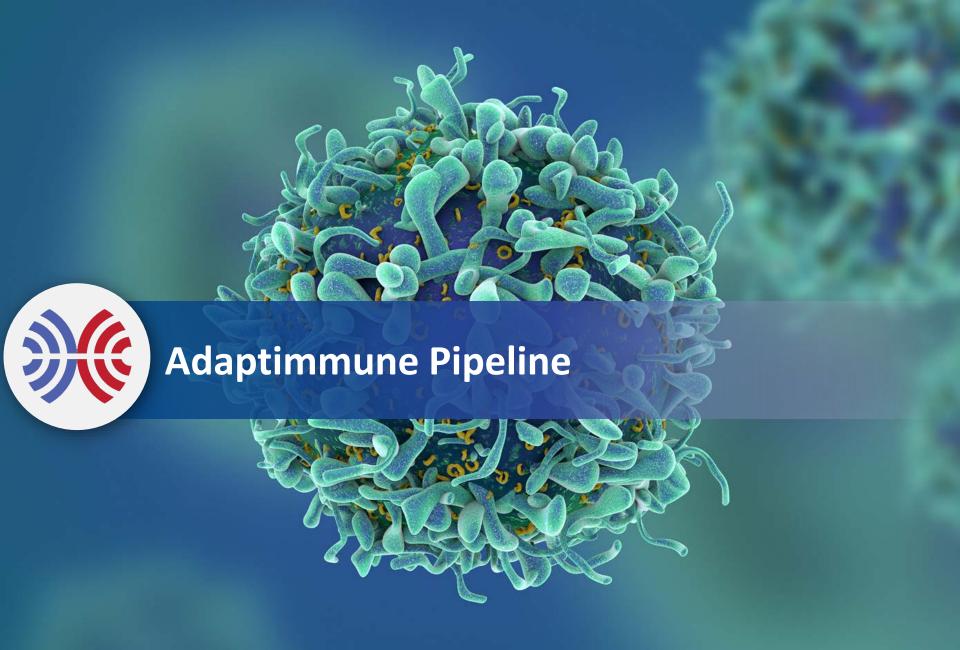
#### MAGE-A4

- IND open (announced January 2017)
- Multi-tumor study in 2017

# **Undisclosed** targets

- 12 targets in research and safety testing
- Assessing 2-3 for key cancers



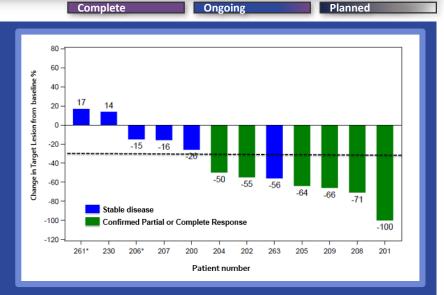


**NY-ESO SPEAR T-cell Development Program: Sarcoma** 

SPEAR target	Indication	Notes	Pre-IND	Phase I / II	Registration
NY-ESO	Synovial sarcoma	Registration			
		Cohort 1 - High NY-ESO +CTX / FLU			
		Cohort 2 - Low NY-ESO +CTX / FLU			
		Cohort 3 – no fludarabine			
		Cohort 4 – modified CTX / FLU			
	Myxoid / Round cell liposarcoma	Pilot study			

#### **NY-ESO SPEAR T-cells in Synovial Sarcoma**

- ~18 months (80 weeks) median survival for cohort 1
- 60% response rate (6/10) in patients receiving target cell dose (50% overall response rate [6/12]) in context of CTX + fludarabine
- Confirmed response seen in 1 of 5 patients with low NY-ESO expression
- Overall, manageable toxicity; highly persistent cells in the presence of fludarabine



#### 2017 Milestones:

Data from synovial sarcoma cohorts 1, 2, and 4; MRCLS pilot study

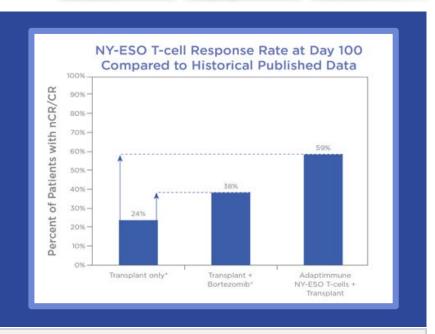


#### NY-ESO SPEAR T-cell Development Program: Multiple Myeloma

SPEAR target	Indication	Notes	Pre-IND	Phase I / II	Registration
NY-ESO	Multiple myeloma	Autologous SCT			
		Combination with anti-PD1 (KEYTRUDA)			
		Comple	ete Ong	oing	Planned

#### **NY-ESO SPEAR T-cells in Multiple Myeloma**

- 3-year overall survival (OS) as of Jan. 2016
- 91 percent (20/22) response rate at day 100
- Median: PFS=19.1 months (11/2015)
- Manageable toxicity, highly persistent cells



#### **2017 Milestones:**

Initiation of combination study with KEYTRUDA®; potential for data in late 2017



NY-ESO SPEAR T-cell Development Programs: Ovarian, Melanoma, and NSCLC

SPEAR target	Indication	Notes	Pre-IND	Phase I / II	Registration
NY-ESO	Ovarian	No fludarabine			
		modified CTX / FLU			
	Melanoma	No fludarabine			
	Non-small cell lung cancer (NSCLC)	modified CTX / FLU			
		Com	plete Ong	going	Planned

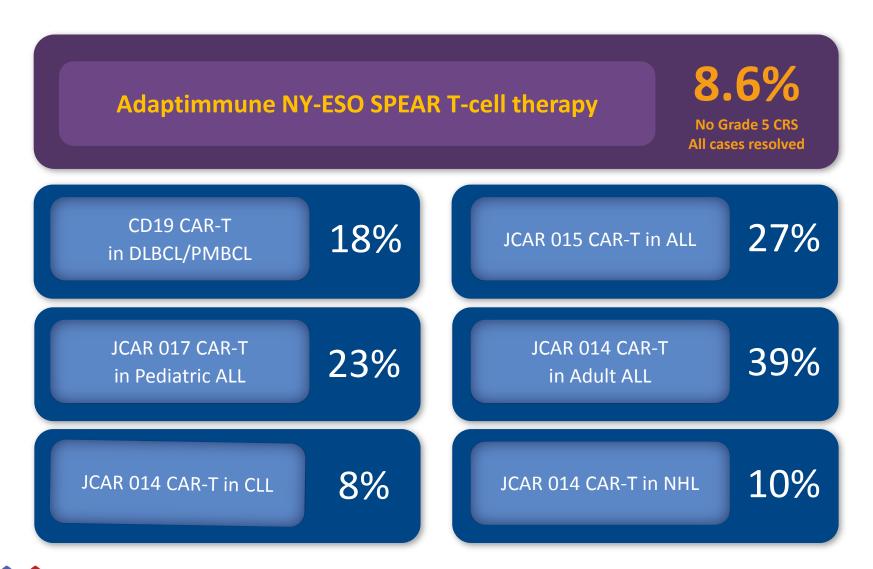
Results of ovarian and melanoma studies with CTX only highlight need for preconditioning regimen including fludarabine

#### **2017** Milestones:

Data from studies in NSCLC and ovarian (with FLU)



## Frequency of Grade 3+ CRS: NY-ESO SPEAR-T vs CAR-Ts





## **Neurotoxicity:** NY-ESO SPEAR-T vs CAR-Ts

NY-ESO SPEAR T-cells: Not associated with the type and severity of neurotoxicity events seen with CAR-T

CD19 CAR-T in DLBCL/PMBCL

JCAR 017 CAR-T in Pediatric ALL

JCAR 014 CAR-T in CLL

JCAR 014 CAR-T in CLL

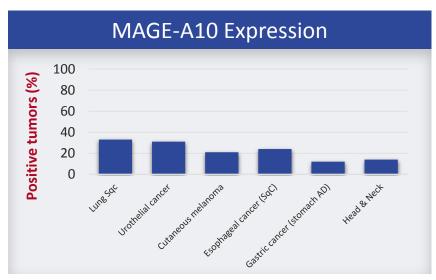
Grade 3 or 4
3% Grade 5

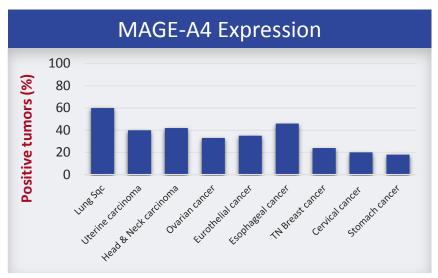
23%
Severe

29% JCAR 015 CAR-T in ALL Grade 3+ 39% JCAR 014 CAR-T in Adult ALL Grade 3+ 10% JCAR 014 CAR-T in NHL Severe



#### MAGE-A10 and -A4: Expressed Across a Wide Range of Tumors





#### **Estimated Annual Deaths**

Source: TCGA Research Network: http://cancergenome.nih.gov, January 2017.

	US <sup>1</sup>	Europe <sup>2</sup>
Urothelial	16,390	52,374
Head and neck	9,570	43,704
Ovarian	14,240	42,716
Melanoma	10,130	22,199
Lung	158,080	353,580
Esophageal	15,690	39,504
Gastric	10,730	107,313



#### MAGE-A10 and -A4 SPEAR T-cell Development Programs: Multiple Cancers

SPEAR target	Indication	Notes	Pre-IND	Phase I / II	Registration
MAGE-A10	Non-small cell lung cancer (NSCLC)	modified CTX / FLU			
	Urothelial (bladder), melanoma, H&N	modified CTX / FLU			
MAGE-A4	Urothelial, melanoma, H&N, ovarian, NSCLC, esophageal, gastric			_	
		Comp	olete Ong	oing	Planned

**2017 Milestones:** 

Data from NSCLC and triple tumor studies of MAGE-A10 SPEAR T-cells

2017 / 2018 Milestones:

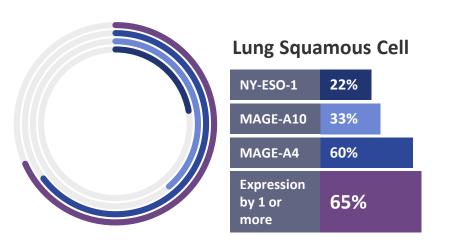
Data from multi-tumor study of

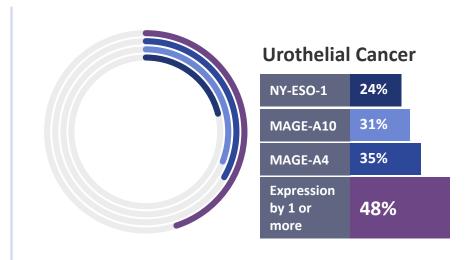
MAGE-A4 SPEAR T-cells



#### **Building a Franchise: Broad Coverage of Cancers with Existing CTA Pipeline**

#### **Tumor Overlap Examples**







#### **Head & Neck Cancer (squamous cell)**

NY-ESO-1	10%
MAGE-A10	14%
MAGE-A4	42%
Expression by 1 or more	44%



#### **AFP SPEAR T-cell Development Program: Hepatocellular cancer**

SPEAR target	Indication	Notes	Pre-IND	Phase I / II	Registration
AFP	Hepatocellular cancer	Modified CTX / FLU			
		Со	mplete Ong	oing	Planned

# AFP Expression 100 80 80 40 20 0 Liver HCC Source: TCGA Research Network: http://cancergenome.nih.gov, January 2016.

#### **Estimated Annual Deaths**

	US <sup>1</sup>	Europe <sup>2</sup>
Liver HCC	27,170	62,152

# 2017/2018 Milestones:

Data from study in hepatocellular cancer

- 1. Source: seer.cancer.gov; http://www.cancer.org/; 2016 data
- 2. Source: eco.iarc.fr/eucan; 2012 data



## **Unmatched Clinical Pipeline** of Affinity Enhanced TCRs

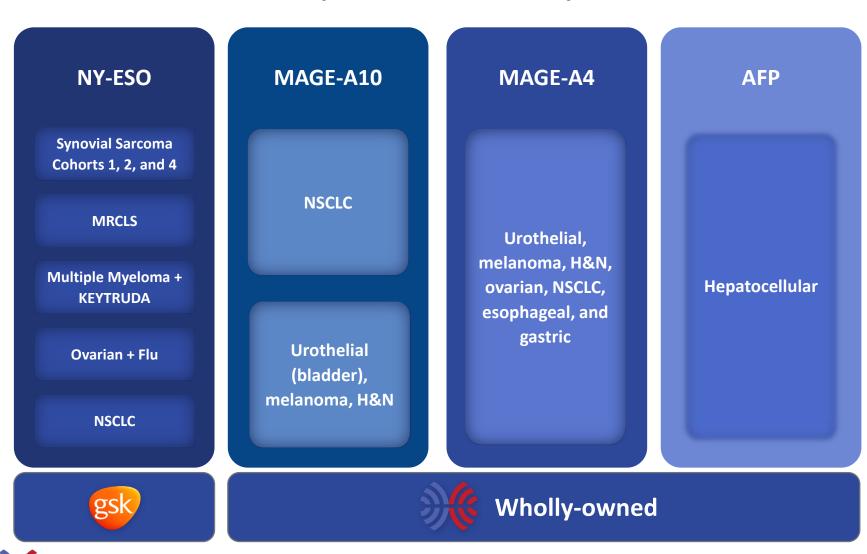
SPEAR target	Indication	Notes	Pre-IND	Phase I / II	Registration trial
NY-ESO	Synovial sarcoma	Registration trial			
		Cohort 1 - High NY-ESO + CTX / FLU			1
		Cohort 2 - Low NY-ESO + CTX / FLU			
		Cohort 3 – no FLU			1
		Cohort 4 – modified CTX / FLU		_	
	Myxoid / Round cell liposarcoma	Pilot study			
	Multiple myeloma	Autologous SCT			
		Combination with anti-PD1 (KEYTRUDA)			
	Ovarian	No FLU			
		Modified CTX / FLU			
	Melanoma	No Flu			
	Non-small cell lung cancer (NSCLC)	Modified CTX / FLU			
MAGE-A10	NSCLC	Modified CTX / FLU			
	Urothelial (bladder), melanoma, H&N	Modified CTX / FLU			
AFP	Hepatocellular cancer	Modified CTX / FLU			
MAGE-A4	Urothelial, melanoma, H&N, ovarian, NSCLC, esophageal, gastric			_	



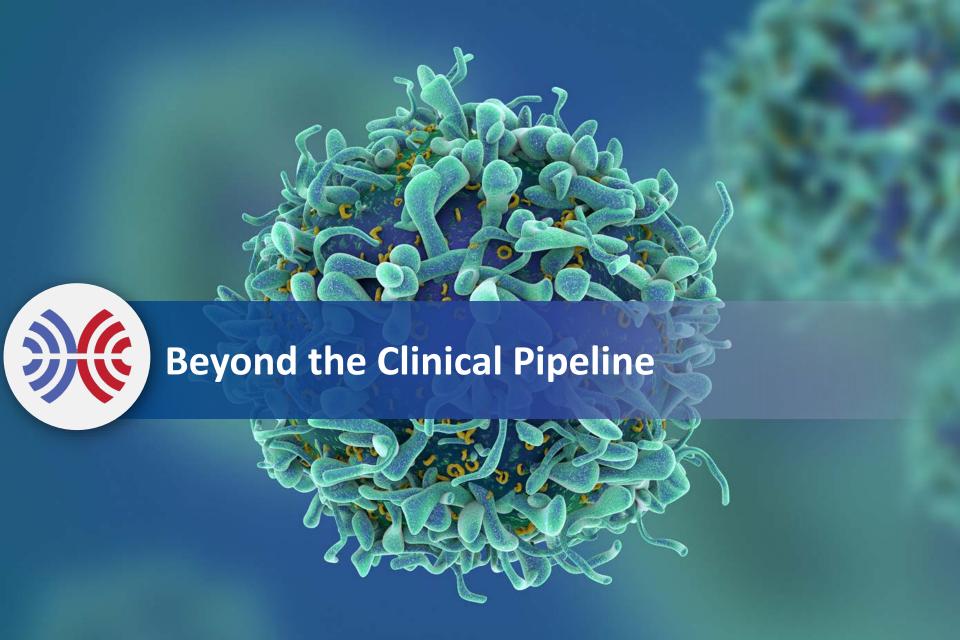
Complete Ongoing Planned

## : A Year of Significant Data Delivery

Potential for Data from Multiple SPEAR T-cell Therapies in 2017 and 2018







## **Leading Innovation** in Engineered T-cell Therapy

#### **Next Generation: Depth and Durability in Solid Tumors**

- Combination studies starting in 2017
- Enhancing resistance to tumor microenvironment: 5 programs and growing
  - ✓ Block effects of immunosuppression (e.g., TGF-β)
  - ✓ Overcoming metabolic restrictions of tumor environment
  - ✓ Other internal programs in development
- Enhancing T-cell potency and function: 11 programs and growing
  - ✓ Enhancement of Class-I restricted CD4 T-cell function
  - ✓ Enhancement of cytotoxic function
  - ✓ Enhancement of epitope spreading
  - ✓ Other internal programs in development
  - ✓ Partnership with Bellicum



## **Leading Innovation** in Engineered T-cell Therapy

#### **Innovative Partnership with Bellicum**



- Staged collaboration to evaluate Bellicum's "GoTCR" switch technology
- Technology could complement our next generation efforts
  - ✓ Provides potential on/off switch to T-cell
  - ✓ May further enhance SPEAR T-cell proliferation, activation and persistence
- Preclinical POC will be completed in 2017
- Potential to proceed into co-development / co-commercialization phase in 2017/2018



## **Leading Innovation** in Engineered T-cell Therapy

#### Allogeneic Approach to TCR T-cell Therapy

Universal Cells

- Partnered with Universal Cells
- Benefits of allogeneic approach include
  - ✓ Allows one manufacturing batch to treat numerous patients
  - ✓ Enhanced control and standardization of manufactured product
  - ✓ Eliminates risk of rejection by host and GvHD
  - ✓ Decreases manufacturing costs
  - ✓ Scalable for unlimited commercial manufacture
- Progenitor cell line evaluated; T-cell differentiation ongoing
- Pre-IND meeting in planning



## Global Technology Network: Partnering with Industry Leaders





## **Advantages** of Adaptimmune's Manufacturing Process

**Robust Expansion** 

Maximum Flexibility

Positive Selection

Serum Free Expansion

**Rapid Turnaround** 

**T-cell Persistence** 

Minimizes vector requirement, no IL-2 or feeder cells

**Cryopreservation possible on both ends of the manufacturing process** 

CD3/CD28 beads; CD4 and CD8 T-cells; no Tregs

Reduced serum dependency for minimizing cost and risk

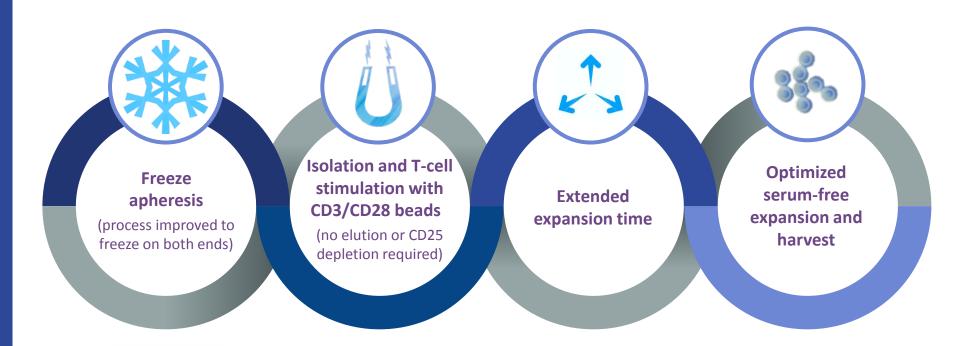
**10-day manufacturing process** 

Retained tumoricidal activity; long-term memory phenotype, minimal exhaustion



## **Cell Manufacturing**

#### **Improved Efficiency over Academic Process**







## **Strong Financial Position**

#### **Third Quarter 2016 Financial Results**

- Financial position as of September 30, 2016
  - \$140.4 million of cash and cash equivalents
  - \$47.1 million of short-term deposits
  - Combined represents a total liquidity position of \$187.5 million\*
- Will fund operations through mid-2018\*\*

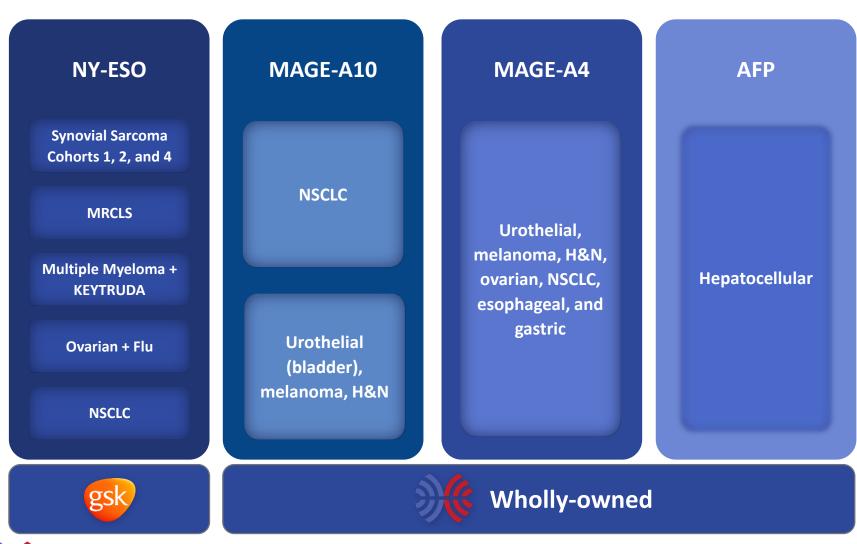
<sup>\*\*</sup> Guidance excludes any new business development and is based on current company assumptions



<sup>\*</sup> Total liquidity position is a non GAAP financial measure, which is explained and reconciled to the most directly comparable financial measures prepared in accordance with GAAP

## : A Year of Significant Data Delivery

Potential for Data from Multiple SPEAR T-cell Therapies in 2017 and 2018







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