

**Corporate Presentation** 



# **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 Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC) on March 13, 2017 and our other SEC filings.

We urge you to consider these factors carefully in evaluating the forward-looking statements herein and you 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.



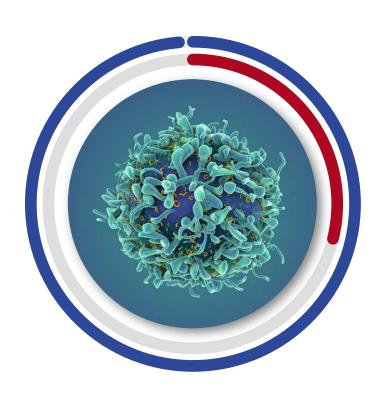
# Adaptimmune Positioned for Delivery in 2017/18

- Three wholly-owned INDs open (MAGE-A10, -A4 and AFP) in 8 tumor types
  - Momentum in patient screening and recruitment
  - Initial data likely 2H 2017 and 1H 2018
- Significant progress with NY-ESO\* program
  - Plan to initiate registration study around end 2017, subject to regulatory process
  - Initial data from MRCLS, NSCLC and ovarian studies likely 2H 2017 and 1H 2018
  - Initiation of combination study with Keytruda®



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

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



Nearly all proteins are available to TCRs

Access to extra- and intracellular proteins

**TCRs** 

Potentially 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



# T-cells Play Critical Role in Cell-Mediated Immunity TCRs Eliminate Damaged/Diseased/Foreign Cells, but Cancer Evades Detection

- Cells display status by presenting peptides on their surface using HLA molecules
  - Peptides in peptide-HLA complexes change if cell is damaged, cancerous or infected
- T-cells generally only recognize different "non-self" cells due to thymic selection
- T-cell recognition based on affinity of the TCR to the target peptide-HLA complex
- Multiple TCRs bind target peptide-HLA, which cluster to form an immune synapse
- T-cells release cytolytic granules, inducing target cell death
- However, T-cells have trouble recognizing cancer cells as targets
  - Cancer peptides are derived from normal, "self" proteins
  - Thymic selection deleted T-cells with high affinity to "self" proteins including cancer peptides
  - Cancer cells express a lower number of targets



# 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

- Largely exclusive to tumor tissue; shown to be good targets
- 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)
- Planned registration studies in synovial sarcoma



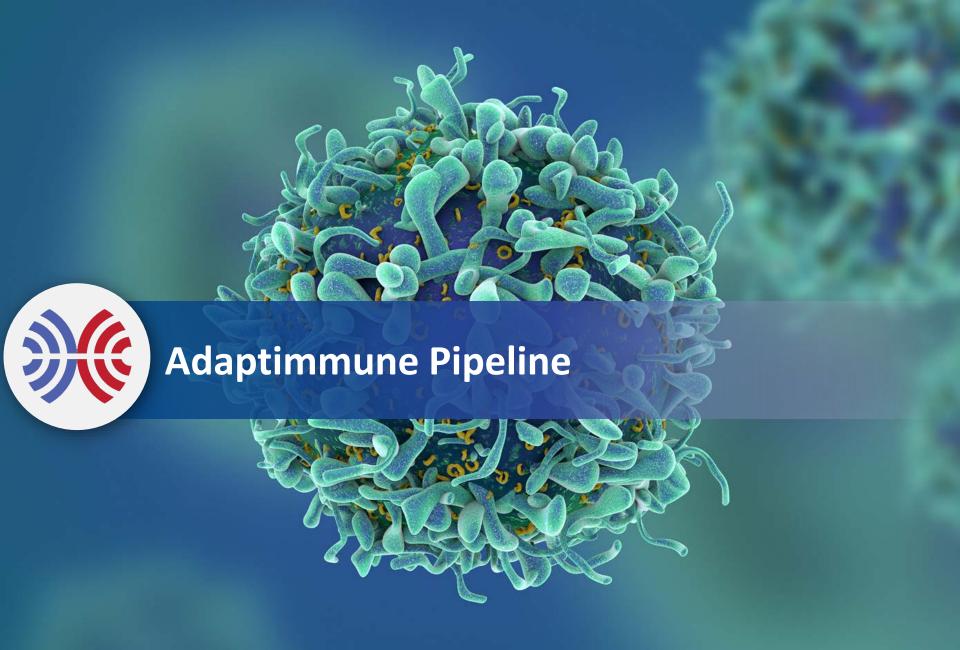
MAGE-A10

- 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



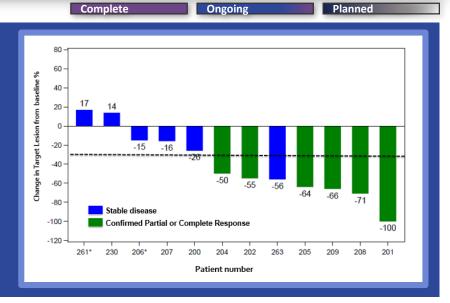


**NY-ESO SPEAR T-cell Development Program: Sarcoma** 

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



#### **2017/2018 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



#### **2017/2018 Milestones:**

Initiation of combination study with KEYTRUDA®; data in 2018



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			ı
		modified CTX / FLU			
	Melanoma	No fludarabine			l
	Non-small cell lung cancer (NSCLC)	modified CTX / FLU			
		Com	plete On	going	Planned

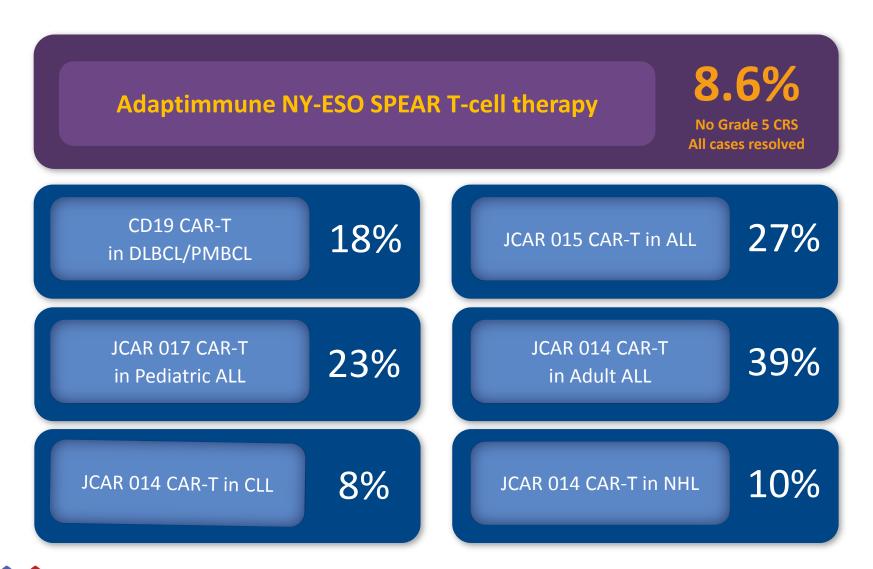
Results of ovarian and melanoma studies with CTX only highlight need for preconditioning regimen including fludarabine

**2017/2018** 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

Severe

NY-ESO SPEAR T-cells: Not associated with the type and severity of neurotoxicity events seen with CAR-T 34% CD19 CAR-T 29% JCAR 015 CAR-T in ALL in DLBCL/PMBCL Grade 3 or 4 Grade 3+ **3% Grade 5** 39% JCAR 017 CAR-T 23% JCAR 014 CAR-T in Pediatric ALL in Adult ALL

JCAR 014 CAR-T in CLL

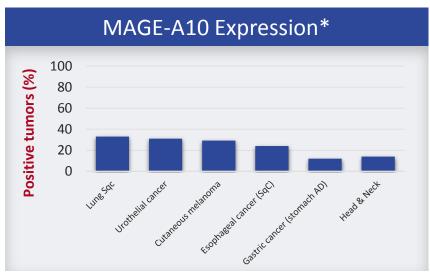
25%
Grade 3-5

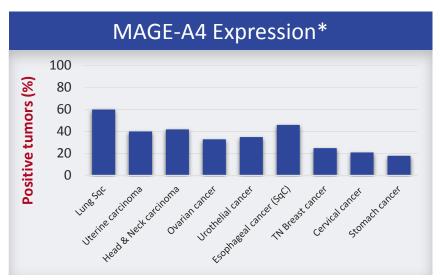
JCAR 014 CAR-T in NHL Severe



Grade 3+

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





#### **Estimated Annual Deaths**

Source: TCGA Research Network: http://cancergenome.nih.gov, March 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		_	_	
		Com	plete Ong	going	Planned

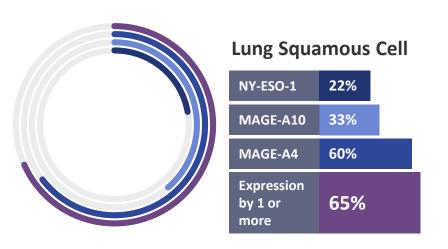
2017/2018 Milestones:
Data from NSCLC and triple tumor studies of MAGE-A10 SPEAR T-cells

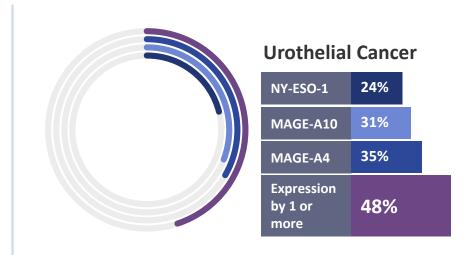
2017/2018 Milestones:
Data from multi-tumor study of
MAGE-A4 SPEAR T-cells



#### **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			
		Co	mplete Ong	oing	Planned

# AFP Expression 100 80 60 40 20 0 Liver HCC

#### **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

Source: TCGA Research Network: http://cancergenome.nih.gov, January 2016.



# **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			
		Cohort 2 - Low NY-ESO + CTX / FLU			
		Cohort 3 – no FLU			
		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			_	

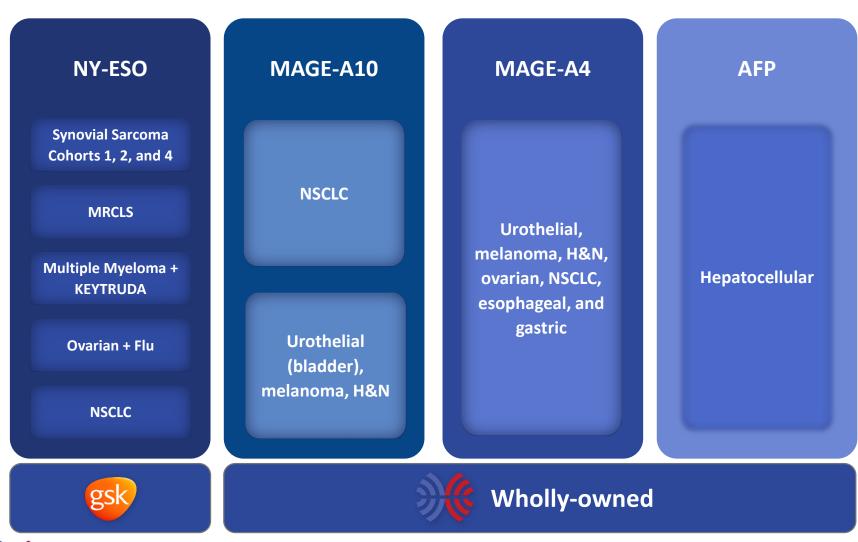


Complete Ongoing

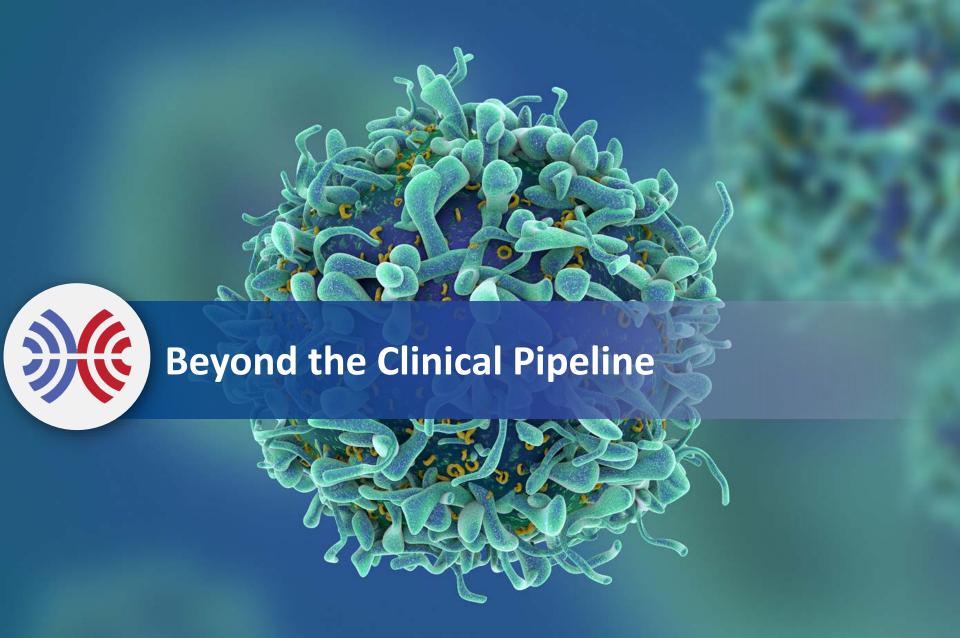
Planned

# : 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

#### **Addressing 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** 

Minimizes vector requirement, no IL-2 or feeder cells

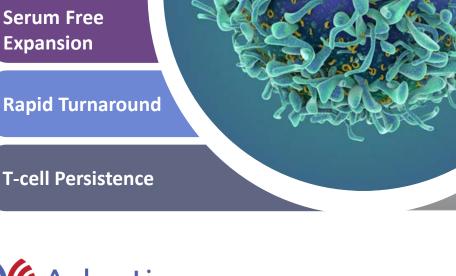
Cryopreservation possible on both ends of the manufacturing process

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

Reduced serum dependency for minimizing cost and risk

**10-day manufacturing process** 

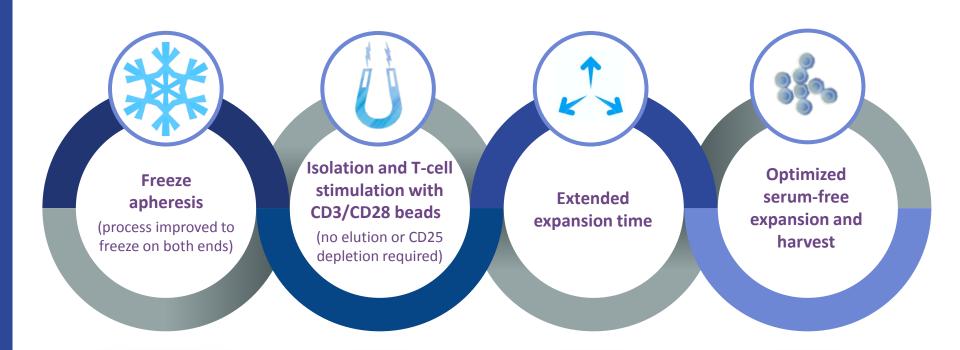
Retained tumoricidal activity; long-term memory phenotype, minimal exhaustion





# **Cell Manufacturing**

### **FDA Allowance to Proceed with Improved Process**







# **Financial Update**

#### **Funds Operations through Mid-2019\***

- Financial position as of December 31, 2016
  - \$158.8 million of cash and cash equivalents
  - \$22.7 million of short-term deposits
  - Combined represents a total liquidity position of \$181.5 million\*\*
- March 2017 public offering (15.7M ADS, \$4.20 per ADS)
  - ~\$61.8 million net proceeds, including impact of underwriters option

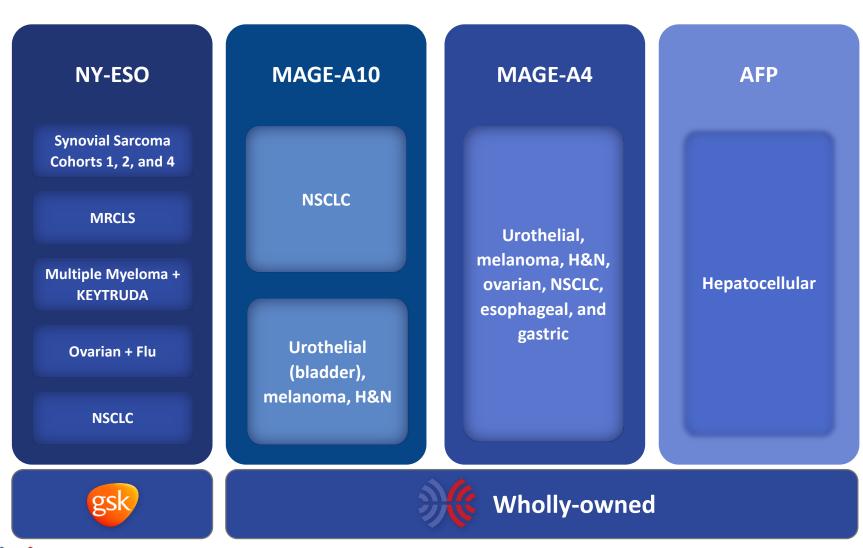
<sup>\*\*</sup> Total liquidity position is a non GAAP financial measure, which is explained and reconciled to the most directly comparable financial measures prepared in accordance with GAAP



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

# : A Year of Significant Data Delivery

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







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