
SPEAR-heading
TCR
Adaptimmune
TRANSFORMING T CELL THERAPY

August 2019

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 August 1, 2019 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.

SPEAR-heading the cancer revolution

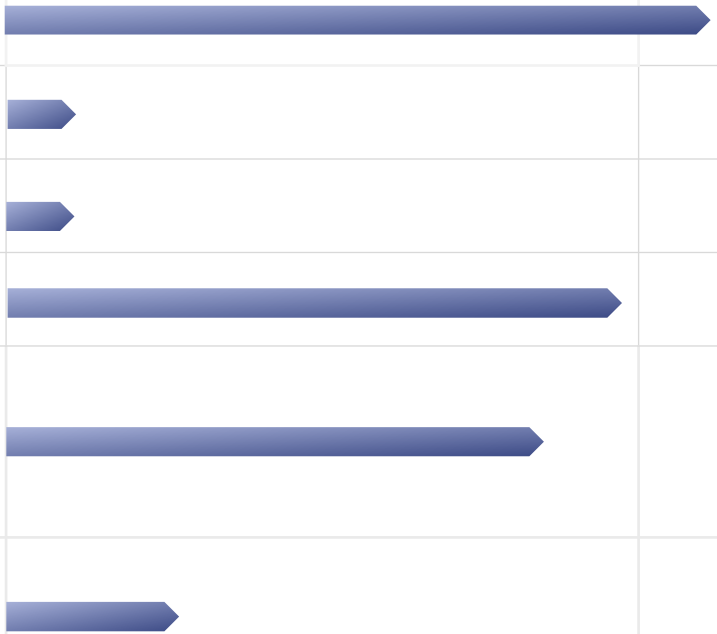
Goal to launch the first TCR T-cell therapy in 2022

Unparalleled breadth of TCR T-cell expertise and products

Initiated late stage development with SPEARHEAD-1 in sarcomas

Pilot trials continue to inform translational learning, study next-gen and other approaches

Target	Study (product)	Indications	Pilot studies	Phase 2/3
MAGE-A4	SPEARHEAD-1 (ADP-A2M4)	Synovial sarcoma MRCLS		
	Radiation sub-study* (ADP-A2M4)	Multiple solid tumors**		
	SURPASS (ADP-A2M4CD8)	Multiple solid tumors**		
	Pilot study (ADP-A2M4)	Multiple solid tumors**		
MAGE-A10	Pilot study‡ (ADP-A2M10)	NSCLC Bladder Melanoma Head & neck		
AFP	Pilot study (ADP-A2AFP)	Hepatocellular carcinoma		



* Site specific protocol amendment with MD Anderson Cancer Center

** Bladder, Melanoma, Head & Neck, Ovarian, NSCLC, Esophageal, Gastric, Synovial sarcoma, MRCLS

‡ Enrollment in the ADP-A2M10 trials closing by end of 2019

Goal to be first & best in class with 2022 launch in sarcoma

Focused on lead program and converting activity into responses in other indications

- World class T-cell manufacturing capability
- Navy Yard from first ever product to 10 patients per month
  - Scalable to ~100s of patients per year
  - Routinely producing target doses

- TCR T-cell regulatory expertise
- Experienced oncology drug development team
- Leading research platform in T-cell therapy in solid tumors supported by expert translational group

- Relationships with leading clinical trial centers in US, EU, and Canada
- Strategic alliance with MD Anderson Cancer Center
- Technology partnerships

* As of 30 June 2019

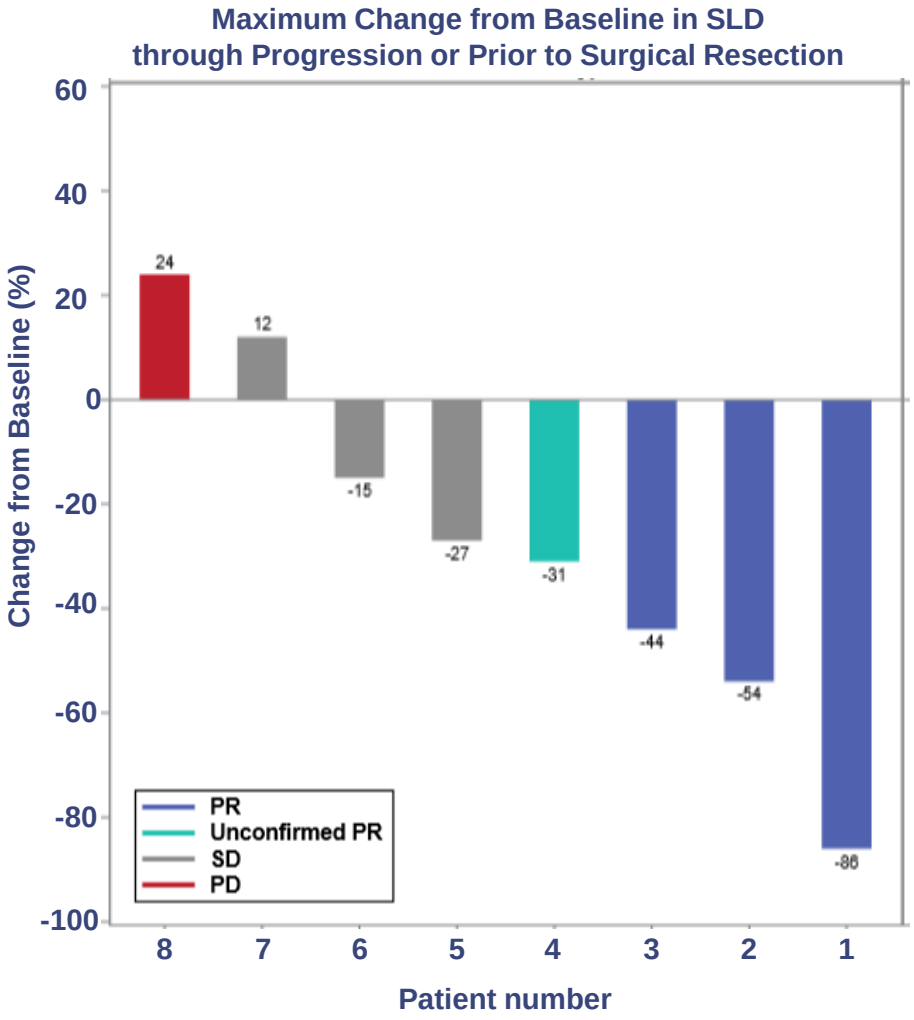
Adaptimmune
TRANSFORMING T CELL THERAPY

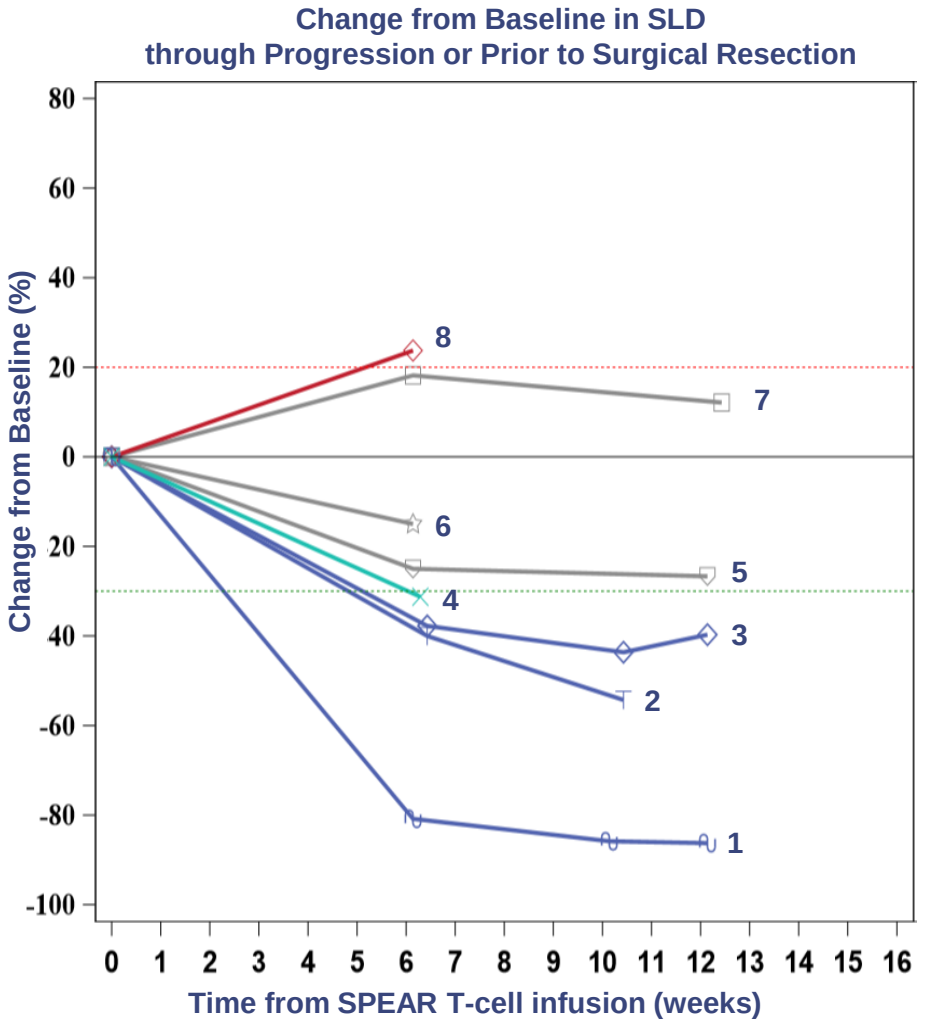
Goal to launch the first TCR T-cell therapy in 2022

Topline sarcoma results

Partial responses in 4 out of 5 synovial sarcoma patients (~10 billion cells)

Tumor shrinkage in nearly all assessed synovial sarcoma patients (ADP-A2M4)



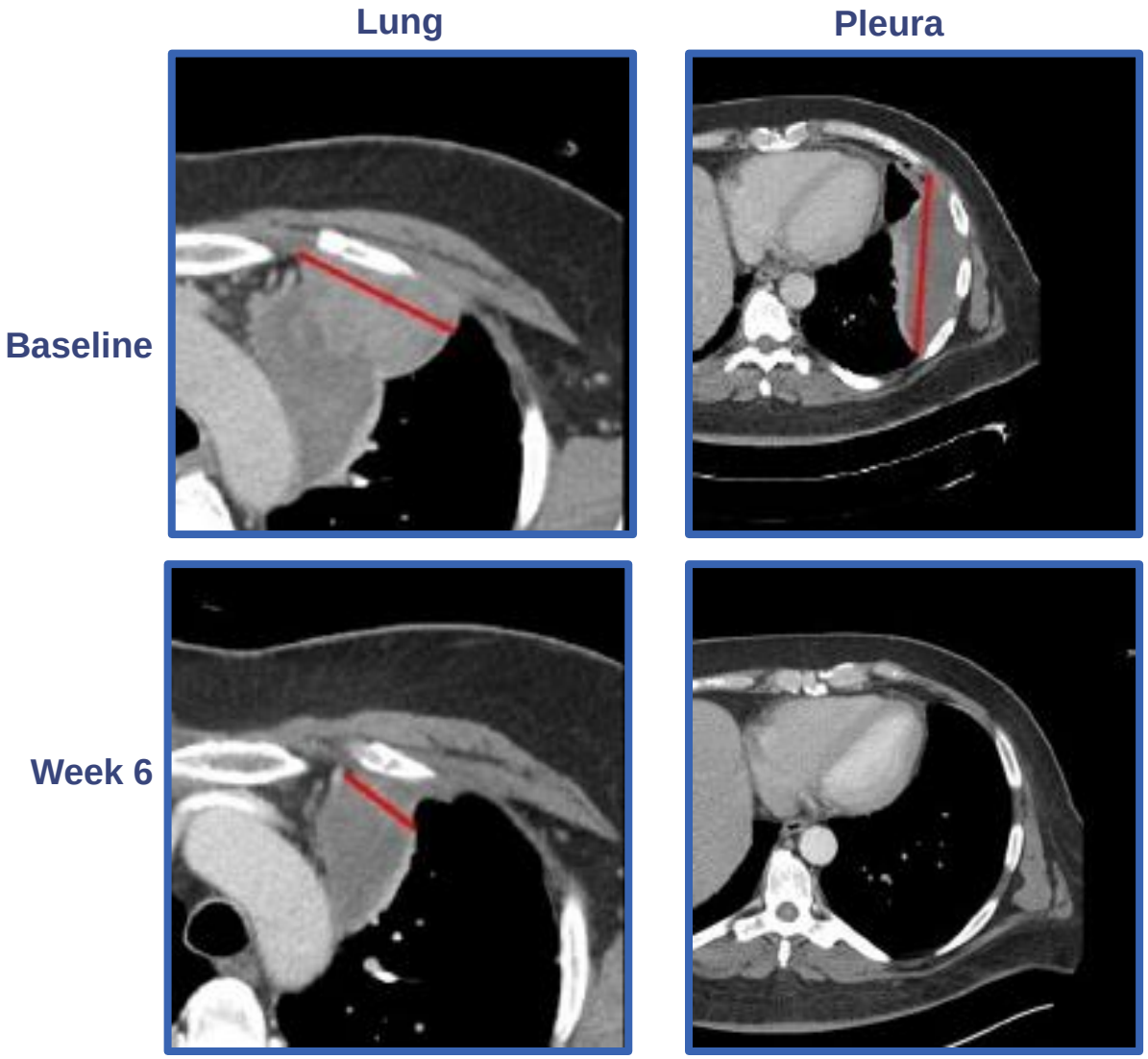


PR=partial response (confirmed); SD=stable disease; PD=progressive disease
Data cut off 30 Apr 2019

Adaptimmune
TRANSFORMING T CELL THERAPY

Confirmed PR: significant tumor reduction

ADP-A2M4 synovial sarcoma Patient #1 with 86% decrease in SLD



86% decrease in SLD and significant symptom improvement

- 53-yr-old male
- Longstanding history of synovial sarcoma
  - Treated with surgery, radiotherapy, and multiple chemotherapy regimens
- High MAGE-A4 expression in tumor
  - Very high disease burden
  - Baseline SLD 24 cm
- ~10 billion SPEAR T-cells
- Did well post-infusion
  - Grade 1 CRS
- Baseline scans:
  - Very extensive disease in the lung and pleural based tumor masses
- Week 6 scans:
  - Dramatically smaller tumor bulk with one very large pleural based lesion having disappeared

SLD=Sum of longest diameters; CRS=cytokine release syndrome
Data cut off 30 Apr 2019

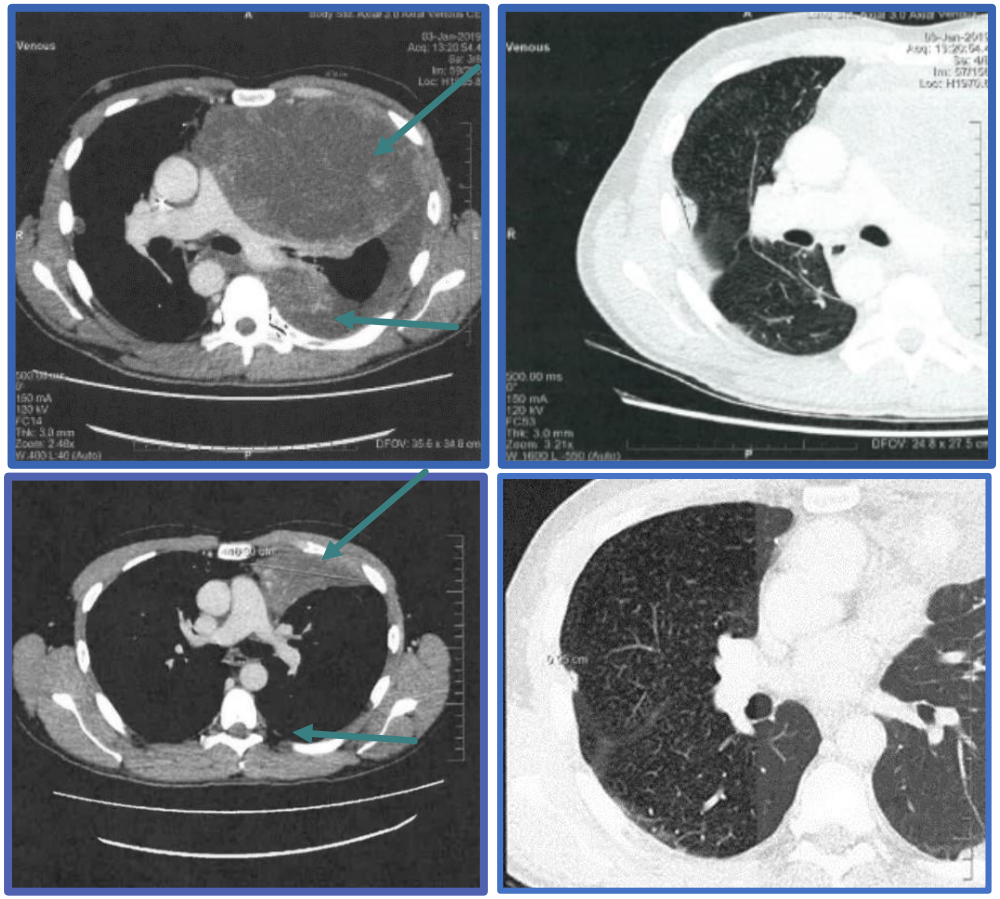
Confirmed PR: bulky tumor almost resolved

ADP-A2M4 synovial sarcoma Patient #3 with 44% decrease in SLD

Lung

Baseline

Week 12



44% decrease in SLD
shortness of breath disappeared

- 42-yr-old male
- Diagnosed age 25
  - Recently developed metastatic disease
  - Synovial sarcoma may recur after many years of remission
- Moderate MAGE-A4 expression
  - Large disease burden
  - Baseline SLD 20 cm
- ~10 billion SPEAR T-cells
- Did well post-infusion
  - Grade 2 CRS and cytopenia
- At baseline
  - Severe shortness of breath due to accumulation of fluid in pleural space
  - Massive tumor (left lung) displacing major blood vessels and compressing right lung (top right scan)
- Week 12 scans
  - Tumor dramatically decreased and non-target lesion gone (lower left scan)
  - Patient lung expanded; shortness of breath disappeared (bottom right scan)

SLD=Sum of longest diameters; CRS=cytokine release syndrome
Data cut off 30 Apr 2019

Safety with SPEAR T-cells

Patients treated with ADP-A2M4, ADP-A2M10, and ADP-A2AFP (n=44)*

Most adverse events consistent with those typically experienced by cancer patients undergoing cytotoxic chemotherapy or other cancer immunotherapies*

Two reports of CRS ≥ Grade 3 for an incidence of ~4.5%*

Incidence rate for all CRS (any grade) is ~39%*

Two SAE reports (one each in the ADP-A2M10 and ADP-A2M4 trials) for severe aplastic anemia, both patient died of complications**

One SAE report of Grade 3 neurotoxicity. The patient subsequently died of a stroke that the Company believes was unrelated to SPEAR T-cell therapy**

Protocol amended for all trials to change eligibility criteria and revert to lower dose of cyclophosphamide

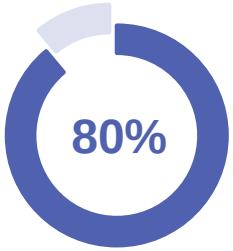
Favorable benefit:risk profile in synovial sarcoma and other indications

* As of April 5, 2019 for ADP-A2AFP and April 15, 2019 for ADP-A2M4 and ADP-A2M10

** Since April 2019 data cut-off dates*: Reported during the Q2 financial results and business update on August 1, 2019

Goal to launch first TCR T-cell product in 2022

Compelling responses in synovial sarcoma with ADP-A2M4



Responses in synovial sarcoma

- Partial responses in 4 out of 5 patients treated with ~10 billion cells
- Tumor shrinkage in nearly all patients assessed to date

SPEARHEAD-1 trial 2H 2019

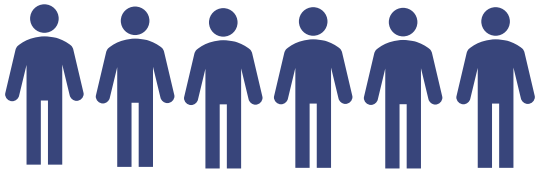
- 60 patients with synovial sarcoma or MRCLS
- Single-arm, Phase 2 study in more than 20 centers (North America & EU)

Data cut off 30 Apr 2019

Significant unmet medical need for sarcoma patients

Focused on bringing transformative therapy to patients with limited options

Current addressable US and EU patients [a]



~ 5,000
Synovial and MRCLS

~30 years old
At diagnosis

~35-50 years old
median age of diagnosis

~ 50%
5-year survival rate

Current treatment

Chemotherapy

↓

Targeted Therapies

↓

Surgical Resection (often radical) [b]

↓

Significant Unmet Need

Potential Treatable Patients (US)

First line Chemotherapy

↓

90% progress to second line

↓

45% HLA+

↓

65% [c] MAGE A4+

Total Eligible Patients

a - for relapsed/refractory synovial sarcoma and MRCLS
b – goal of treatment is to convert unresectable to resectable; surgery can be significant/radical
c – based on blended rate of expression in both subtypes

Adaptimmune
TRANSFORMING T CELL THERAPY

Beyond sarcoma
Antitumor activity and getting to durable responses

Transforming activity into durable responses

Improving SPEAR T-cell activity for cancer patients

Activity in non-sarcoma solid tumors

ADP-A2M4 (5 billion^{+} cells)

- Tumor shrinkage in 1 melanoma (-40%)* and 1 ovarian (-9%) patient

ADP-A2M10 (5 billion^{+} cells)‡

- 2 lung patients had reduced target lesions (-28%** and -6%)

ADP-A2AFP (1 billion cells)

- Transient serum AFP decrease and tumor shrinkage in 1 patient

Translational learnings what matters

- Dose
  - Higher dose or re-dosing
- Preconditioning
- Target antigen expression
- Cell fitness
- Cell potency
- Antigen presentation
- Trafficking
- Target

Our goal is to translate activity into responses

- Higher antigen expression
- Potential for redosing
- Manufacturing parameters
- CD8 to increase T-cell killing
- CD8 to promote epitope spreading
- Disrupt tumor microenvironment
- New targets in development

New studies started:

- ADP-A2M4CD8 next-generation SURPASS study
- ADP-A2M4 low radiation sub-study at MD Anderson Cancer Center

* Patient #11 had a -40% maximum change in SLD; best overall response is PD due to new lesions

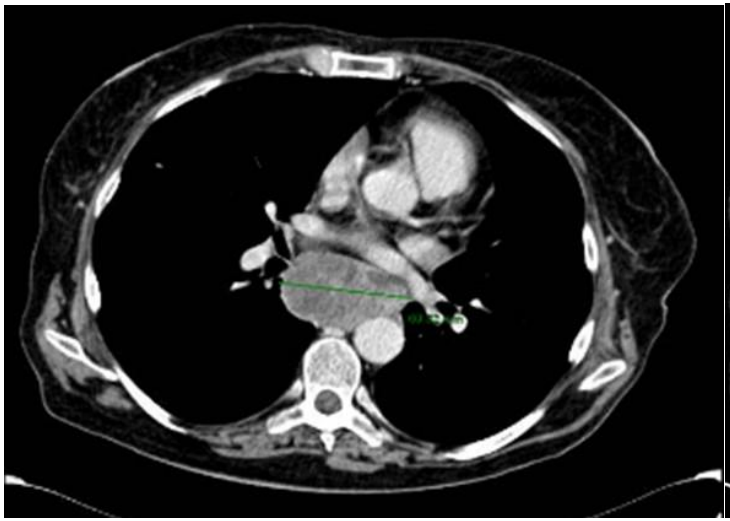
** Patient #1 received second infusion at Week 16; -28% maximum change in SLD is post-second infusion

‡ Enrollment in the ADP-A2M10 trials closing by end of 2019

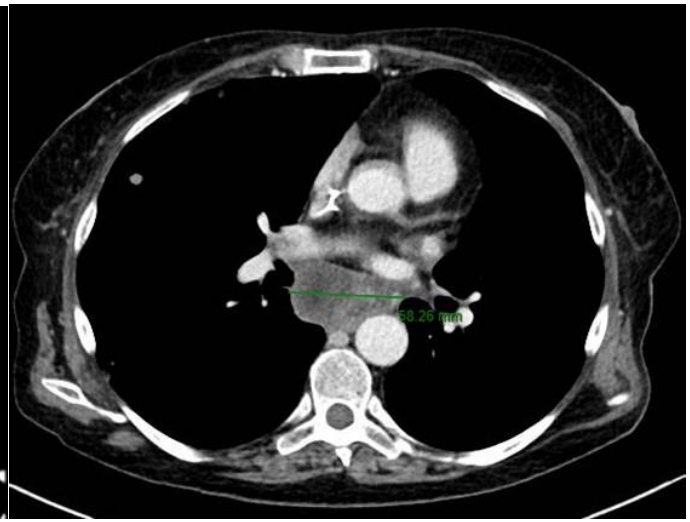
ADP-A2AFP first patient treated in Cohort 2 with 1 billion cells

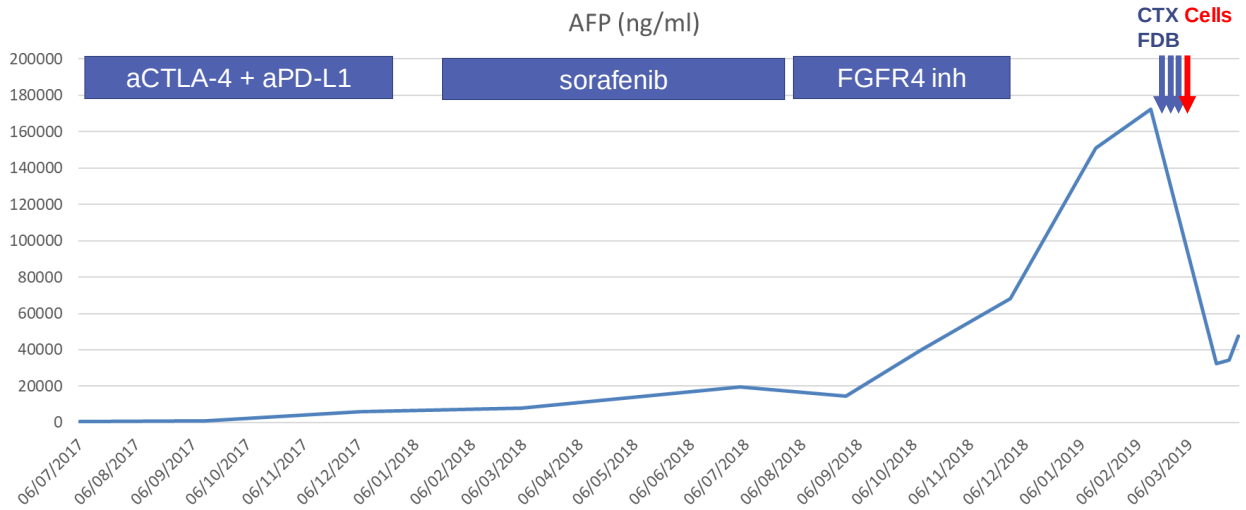
Tumor shrinkage at first scan and strong transient decrease in serum AFP

Baseline



Week 4





Adaptimmune
TRANSFORMING T CELL THERAPY

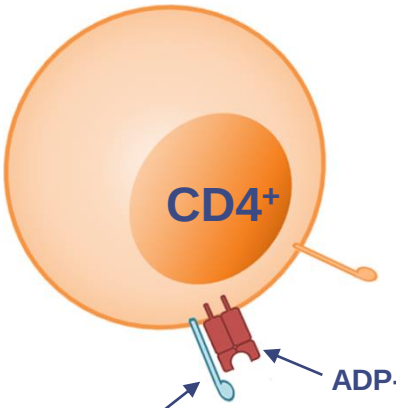
Started SURPASS with next-generation ADP-A2M4CD8 SPEAR T-cells

SPEAR T-cells targeting MAGE-A4 co-expressing CD8α

Preclinical data AACR 2019:

- No evidence of off-target reactivity
- Improved cytokine release of both dendritic cells (DCs) and T-cells in co-culture with MAGE-A4$^+$ cells
- Improved killing of MAGE-A4$^+$ cells (shown below)

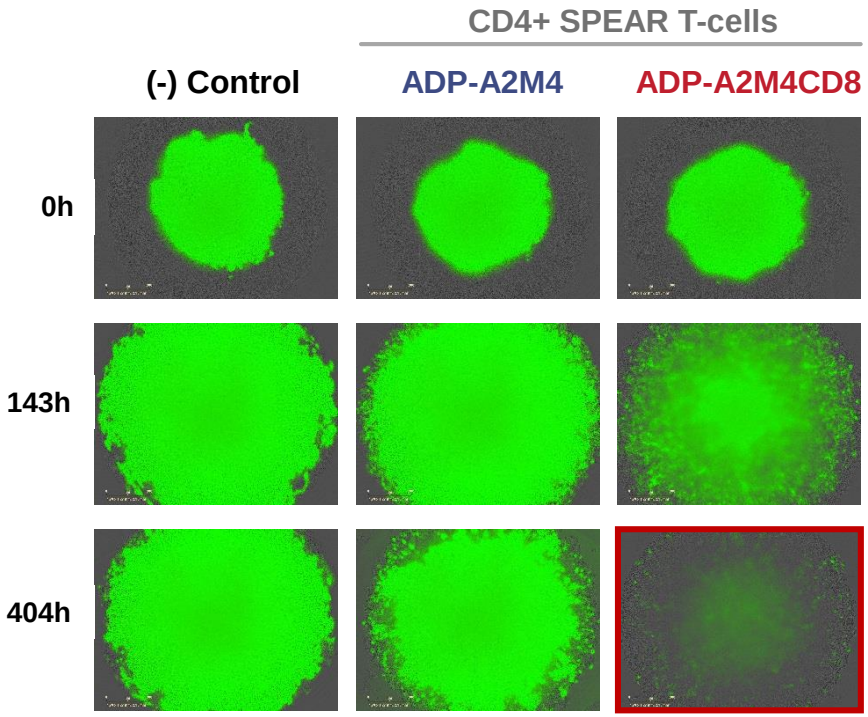
CD4$^+$ ADP-A2M4CD8 SPEAR T-cell



CD4 co-receptor Does not stabilize the TCR target interaction, so no killing – but does bind to DCs

ADP-A2M4 SPEAR TCR

CD8α co-receptor Stabilizes interaction when binding to target cell to enable killing



Adaptimmune
TRANSFORMING T CELL THERAPY

Started radiation sub-study ADP-A2M4 with MD Anderson Cancer Center

Improve tumor trafficking

- SPEAR T-cells could be more effective if tumor infiltration increased
  - Preclinical data shows low dose radiation may improve T-cell penetration into tumors*
- Radiation sub-study of ADP-A2M4 to be conducted at MD Anderson Cancer Center
- Up to 10 subjects to be treated
- Primary endpoint: safety
- Secondary endpoint: response
- Radiation
  - 7Gy (low dose) per lesion or isocenter
  - Maximum of 5 lesions or isocenters
  - Administered prior to lymphodepletion

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

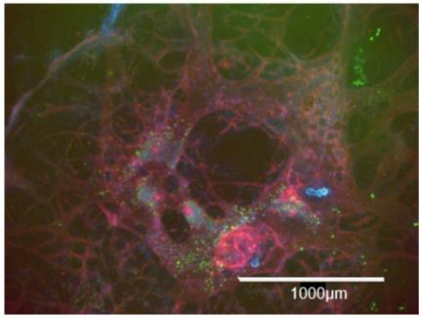
*Barsoumian, 2018; DeSelm, 2018

Significant progress with our allogeneic program

We can produce T-cells from stem cells that respond to cancer targets

Significant progress with stem-cell-derived T-cells

- T-cell marker expression mimics mature T-cells
- Tumor antigen-specific activation via SPEAR TCR
- After stimulation, stem-cell derived T-cells can
  - Produce cytokines
  - Produce and release lytic granules
- Adaptimmune process does not use human serum or stromal cell lines
  - Enabling scale-up and GMP manufacture of edited off-the-shelf lines



CD34 (red) CD3 (green) nuclei (blue)

Can be used with any engineered T-cell (TCR and CAR-T)

This source of T-cells, combined with our engineering expertise, enables a new generation of off-the-shelf T-cell therapies

Looking forward

Data from all programs over next 12 months

2H 2019

- SPEARHEAD-1 study start ✓
- SURPASS study start ✓
- Radiation study start ✓
- Further data from ADP-A2M10 trials
- Further data from ADP-A2M4 trials outside sarcoma

1H 2020

- Durability of sarcoma responses
- ADP-A2AFP data update
- Safety and response data from SURPASS study
- SPEARHEAD-1 interim futility

Beyond 1H 2020

- Allogeneic program data update
- Next targets into clinic
- Data from SPEARHEAD-1
- Data from other programs


SPEAR-heading
TCR
Adaptimmune
TRANSFORMING T CELL THERAPY

August 2019