
SPEAR-heading
TCR
Adaptimmune
TRANSFORMING T CELL THERAPY
November / December 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 November 6, 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

Clear benefit for patients with synovial sarcoma in ADP-A2M4 Phase 1 trial

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

Beyond sarcoma - antitumor activity in 4 solid tumors with ADP-A2M4 and ADP-A2M10 – started first next-gen trial to convert antitumor activity into RECIST responses

Tumor shrinkage at first scan and transient decrease in serum AFP in first patient treated with ADP-A2AFP in Cohort 2

Unparalleled breadth of TCR T-cell expertise and products, with potential for expansion beyond TCR

Initiated late stage development with SPEARHEAD-1 trial in sarcomas

Phase 1 trials continue to inform translational learning, next-gen, and other approaches

Target	Trial	Indications	Phase 1	Phase 2/3
MAGE-A4	SPEARHEAD-1 (ADP-A2M4)	Synovial sarcoma MRCLS	→	→
	SURPASS (ADP-A2M4CD8)	Multiple solid tumors**	→	
	Phase 1 trial (ADP-A2M4)	Multiple solid tumors**	→	→
	Low-radiation sub-study* (ADP-A2M4)		→	
AFP	Phase 1 trial (ADP-A2AFP)	Hepatocellular carcinoma	→	→

ADP-A2M10 Phase 1 trials will complete enrollment by end of 2019

* Site specific protocol amendment with MD Anderson Cancer Center
** Bladder, Melanoma, Head & Neck, Ovarian, NSCLC, Esophageal, Gastric, Synovial sarcoma, MRCLS (myxoid/round cell liposarcoma)

Adaptimmune SPEAR T-cell trials at leading clinical centers

Building the future of T-cell therapy through world-class expertise

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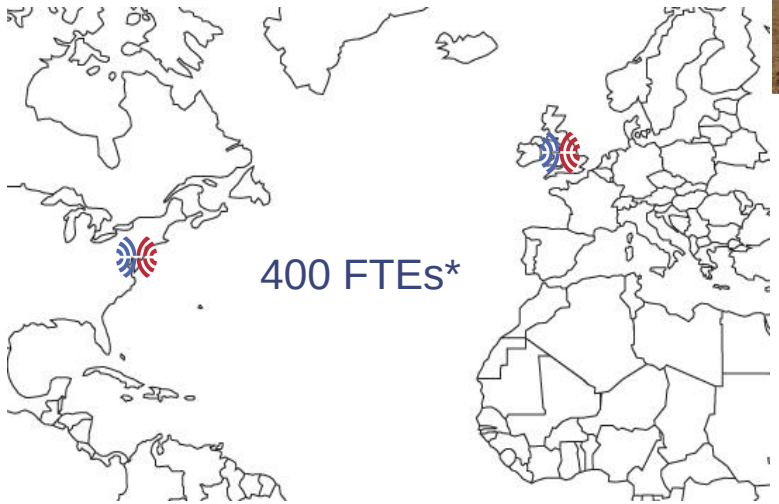
World class capabilities for designing and delivering cell therapies

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

- ✓ Leading research platform in T-cell therapy in solid tumors
- ✓ Experienced oncology drug development team
- ✓ Expert translational group
- ✓ Strategic alliance with MD Anderson Cancer Center
- ✓ T-cell regulatory expertise
- ✓ Fully integrated cell manufacturing scalable to 100s of patients per year

Philadelphia



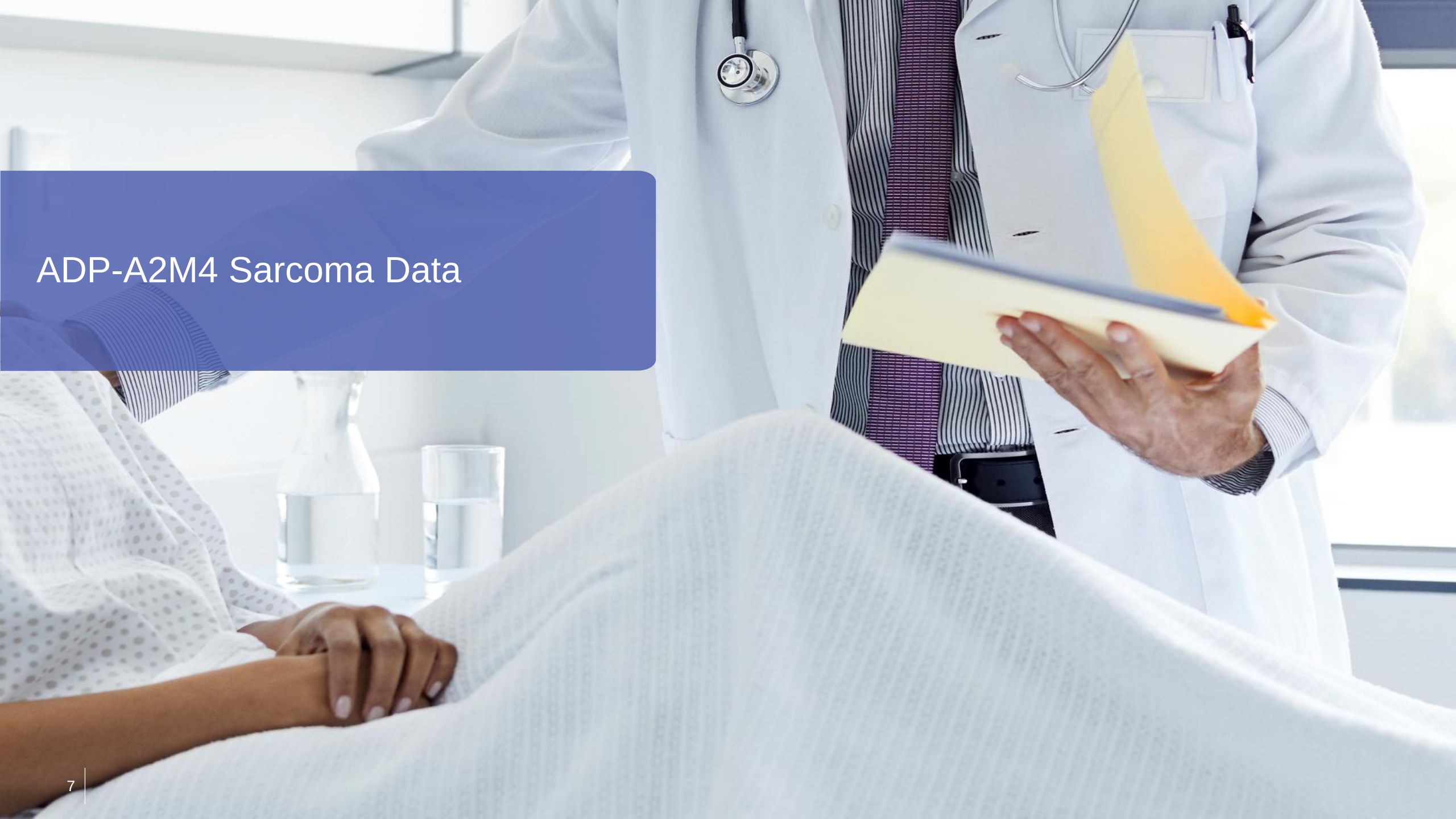
400 FTEs*

Stevenage

Milton Park

* As of 30 September 2019

ADP-A2M4 Sarcoma Data



Significant unmet medical need for sarcoma patients

Focused on bringing transformative therapy to patients with limited options

Synovial Sarcoma [a]

- Most common in adolescents and young adults 15-40 years of age
- Typically localized near large joints, can also occur in the head and neck, mediastinum, and viscera (lung, kidney, etc.)

MRCLS [a]

- Also presents at a younger age ranging from 35-55 years
- Predominantly occurs in the limbs

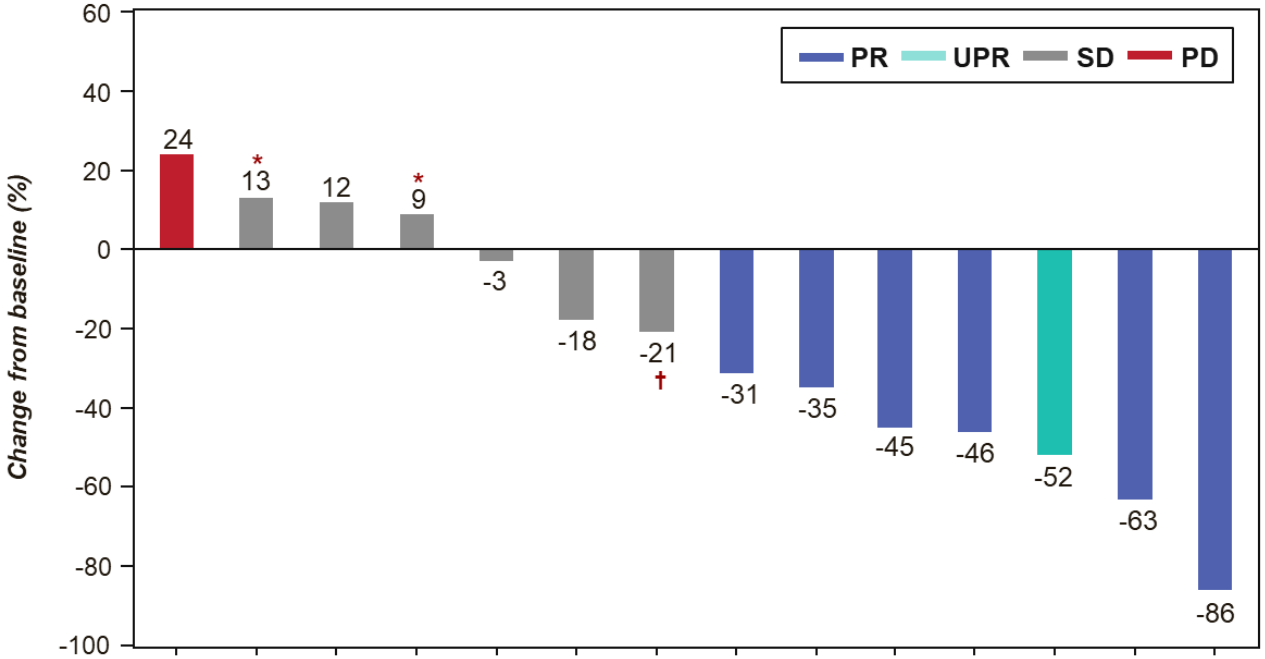
Both cancers associated with poor outcomes – high unmet medical need [b]

- Patients with advanced metastatic disease have highest unmet need
- Prognosis and survival in the range of 18-24 months, with toxicity of currently available therapies also a concern
- Only 1-5% of unresectable tumors are converted to resectable tumors post-treatment with systemic therapies

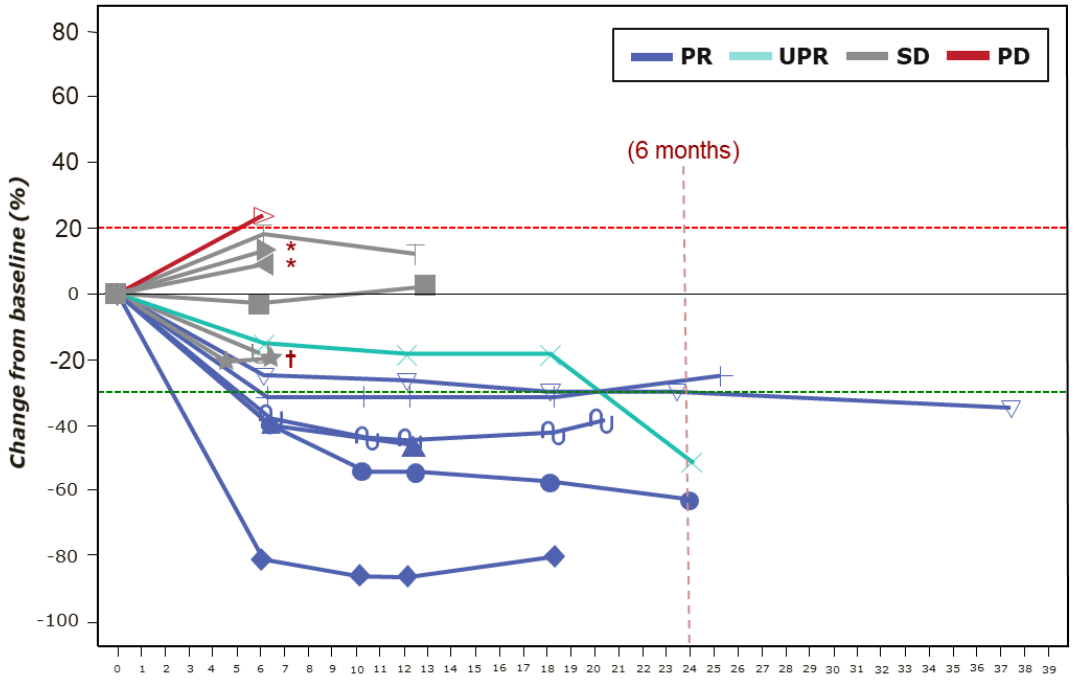
a – Orphanet
b – ADAP data on file (primary market research)
MRCLS=myxoid/round cell liposarcoma

ADP-A2M4 SPEAR T-cells induce clinical responses

Clinical responses in 7 out of 14 patients with synovial sarcoma, and clinical benefit in 13 out 14 patients



Best overall response in 14 patients with post-baseline assessments



Weeks from T-Cell Infusion

ctos®

2019 CTOS Annual Meeting
November 13-16, 2019
Tokyo, Japan

Data cut off 23 Oct 2019 (as reported at CTOS 2019)
*2 patients had single scans †Patient with aplastic anemia

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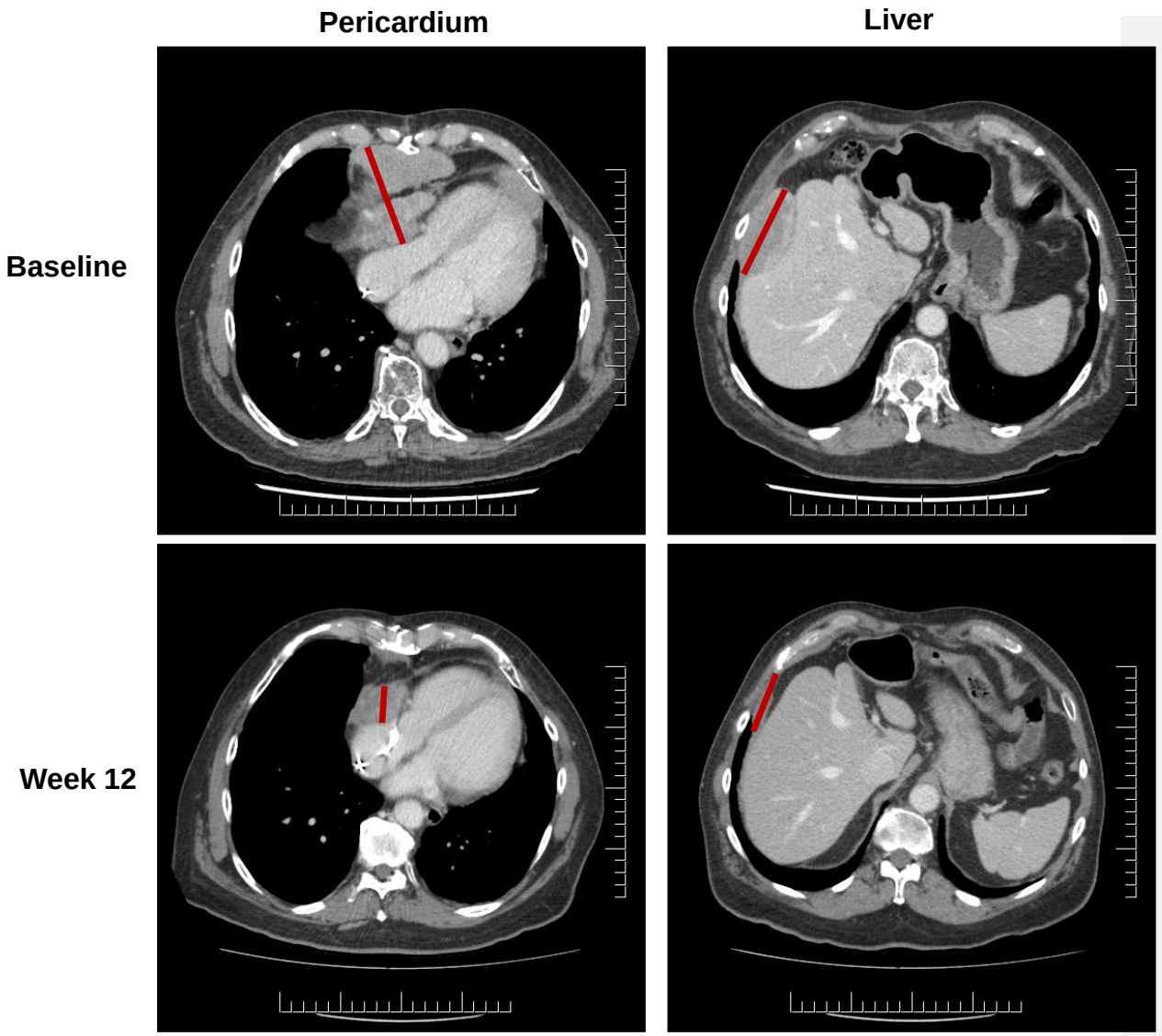
Confirmed PR: significant tumor reduction

ADP-A2M4 patient with synovial sarcoma with 46% decrease in SLD



67-yr-old male

4-yr history of disease

Treated with surgery and radiotherapy

Recurrence in the pericardium treated with debulking and ifosfamide

High MAGE-A4 expression (100% 3+)

Baseline SLD* was 155 mm

Received 9.95 x 10^9 SPEAR T-cells

Baseline scans

Disease in the pericardium and liver

Post-infusion

Grade 2 CRS and cytopenias

Week 12 scans

Reduction in target tumor lesions (confirmed PR by RECIST 1.1)

46%

Decrease in SLD Reductions in lesions around the heart and liver

* SLD=Sum of the Longest Diameter of the target lesions

Data cut off 23 Oct 2019 (as reported at CTOS 2019; note this patient had an unconfirmed PR at ESMO 2019)

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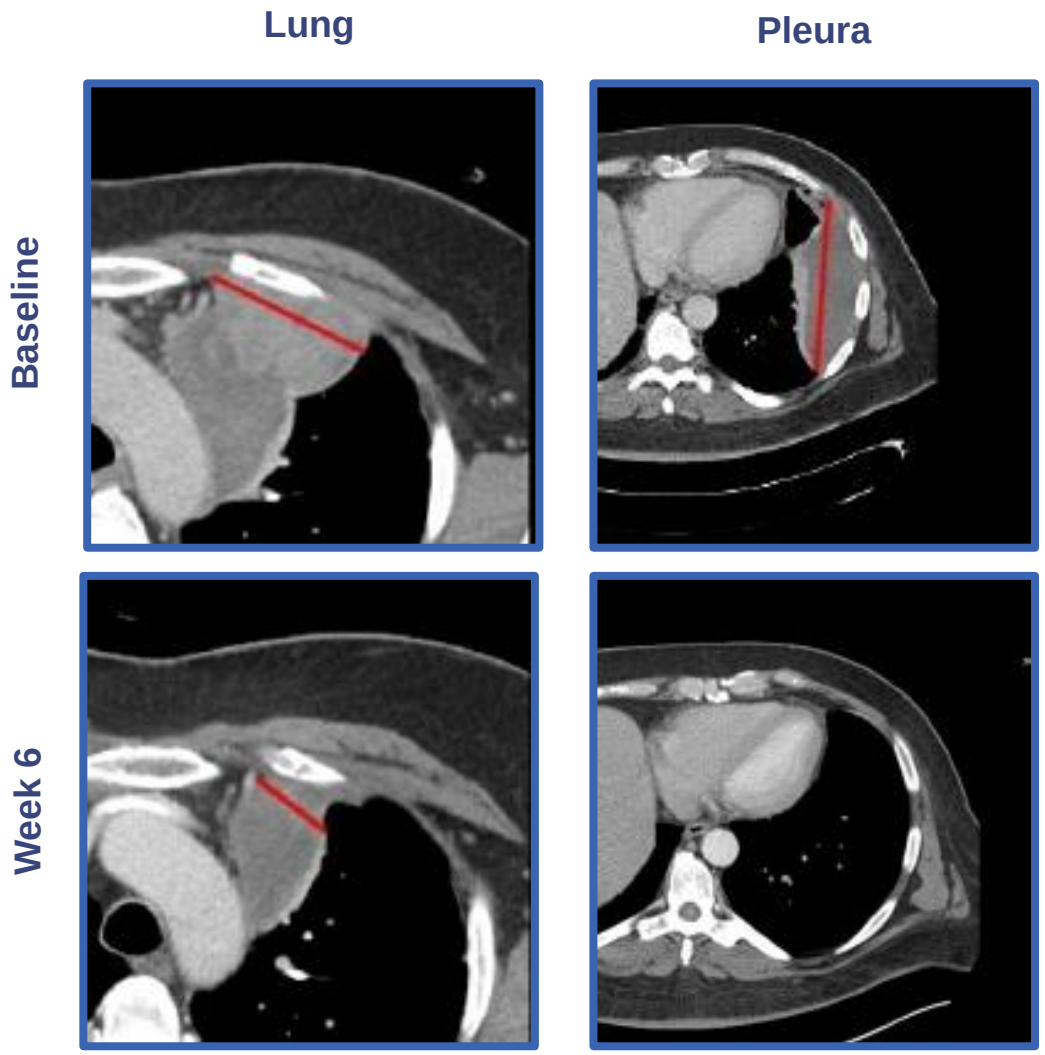
Confirmed PR: significant tumor reduction

ADP-A2M4 patient with synovial sarcoma 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 (100% 3+)

Very high disease burden

Baseline SLD* was 24 cm

~10 billion SPEAR T-cells

Did well post-infusion

Grade 1 CRS and cytopenias

Baseline scans

Very extensive disease in lung and pleural tumor masses

Week 6 scans

Dramatically smaller tumor bulk with one very large pleural lesion having disappeared

* SLD=Sum of the Longest Diameter of the target lesions

Data cut off 30 April 2019 (as reported 06 May 2019)

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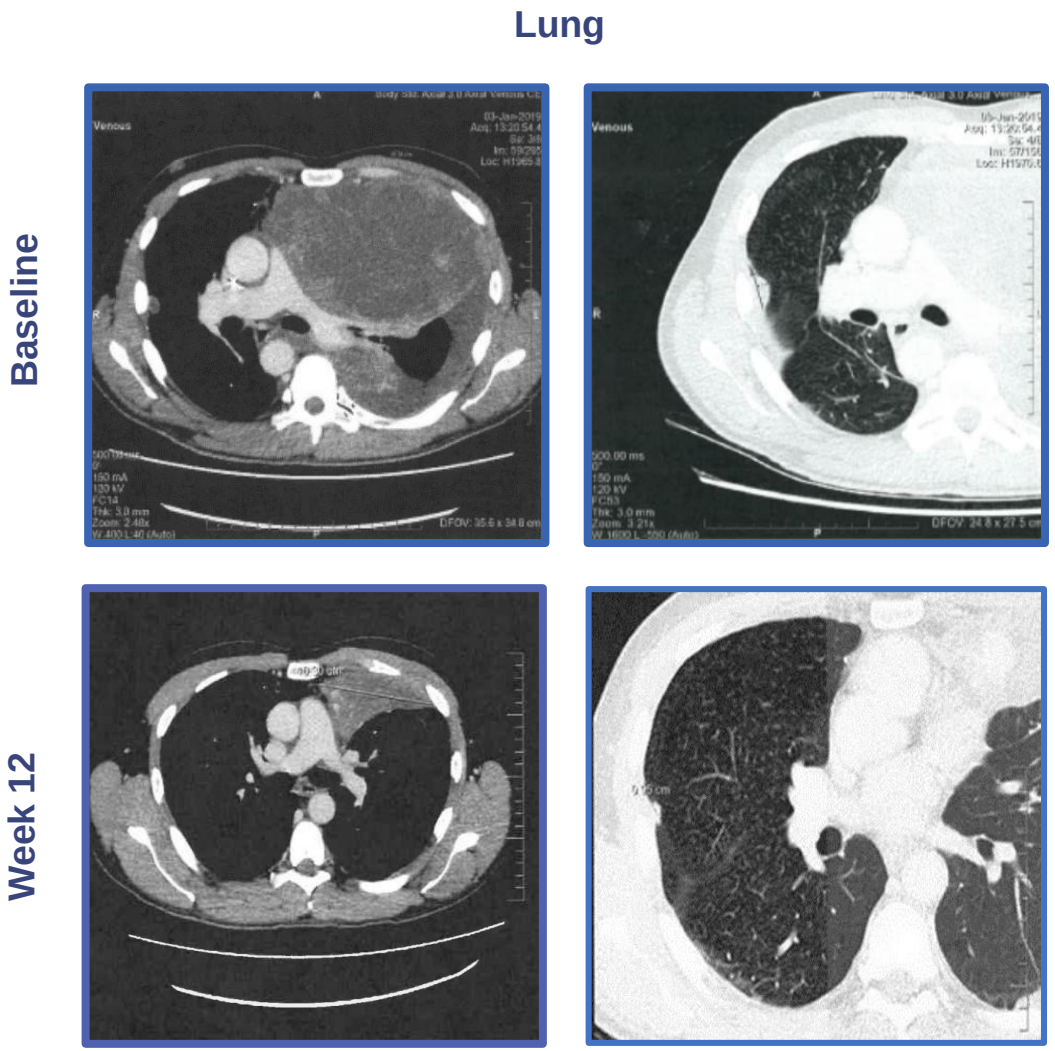
Confirmed PR: bulky tumor almost resolved

ADP-A2M4 patient with synovial sarcoma with 44% decrease in SLD



42-yr-old male

Diagnosed age 25

Recently developed metastatic disease

MAGE-A4 expression moderately high (10% 1+, 35% 2+, 50% 3+)

Large disease burden

Baseline SLD* was 20 cm

~10 billion SPEAR T-cells

Did well post-infusion

Grade 2 CRS and cytopenias

Baseline scans

Severe shortness of breath due to 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)

Lung expanded (bottom right scan); shortness of breath disappeared

44%

Decrease in SLD and shortness of breath disappeared

* SLD=Sum of the Longest Diameter of the target lesions

Data cut off 30 April 2019 (as reported 06 May 2019)

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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*

CRS and neurotoxicity occur at rates consistent with other T cell therapies, and are managed in keeping with current guidelines

Two SAE reports of fatal aplastic anemia (one each in the ADP-A2M10 and ADP-A2M4 trials)**

Protocols for all trials amended modifying eligibility criteria and reverting to a lower, yet clinically effective, dose of cyclophosphamide with an acceptable bone marrow safety profile

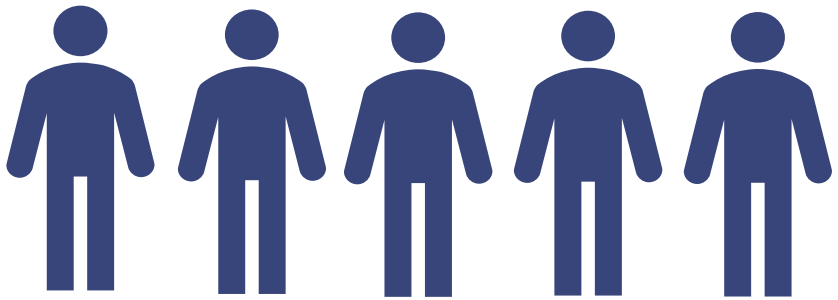
Favorable benefit:risk profile in synovial sarcoma and other indications

* As of April 5, 2019 for ADP-A2AFP and April 15, 2019 for ADP-A2M4 and ADP-A2M10
** As reported during the Q2 financial results and business update 01 Aug 2019

Synovial sarcoma and MRCLS patient population

Goal to launch ADP-A2M4 in sarcoma in 2022

US and EU patients [a]



~ 5,000

Synovial and MRCLS

Potential Treatable Patients (US)

- Resection if localized disease
- First line Chemotherapy
- 90% progress to second line
- 45% HLA^{+}
- 65% [b] MAGE A4^{+}
- **Total Eligible Patients**

a - for relapsed/refractory synovial sarcoma and MRCLS
b - based on blended rate of expression in both subtypes
MRCLS=myxoid/round cell liposarcoma

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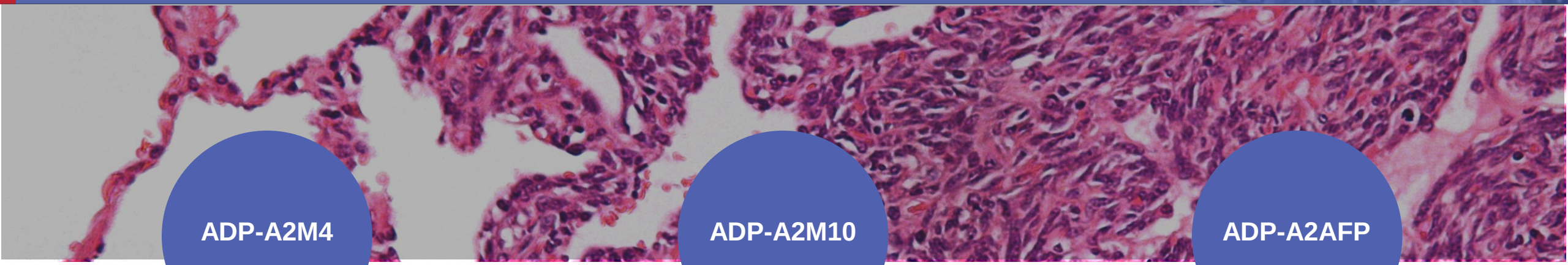
Beyond Sarcoma

Antitumor activity & getting to durable responses

Antitumor activity in indications beyond sarcoma



ADP-A2M4

Tumor shrinkage occurred in:
One melanoma patient (-40% [10B])[a],
Two ovarian patients
(-9% [5.7B][a] and -27% [1B][b])

ADP-A2M10

Two lung patients had reduced target lesions (-28%* and -6% [5.2B])[c]

ADP-A2AFP

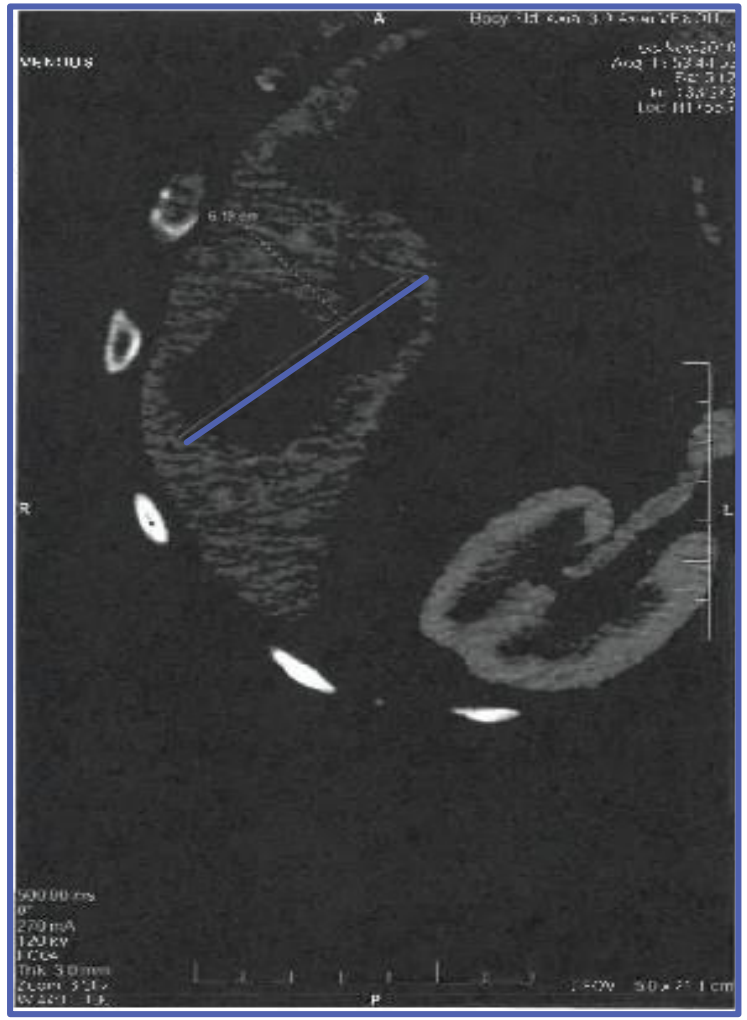
Transient serum AFP decrease and tumor shrinkage in one patient

*Patient received second infusion at Week 16; post-baseline scans presented are after second infusion; first infusion 6B, second was 5.2B
Data cut offs: a: 30 Apr 2019 (as reported on 06 May 2019); b: 02 Aug 2018 (as reported at ESMO 2018); c: 26 Apr 2019 (as reported on 06 May 2019)

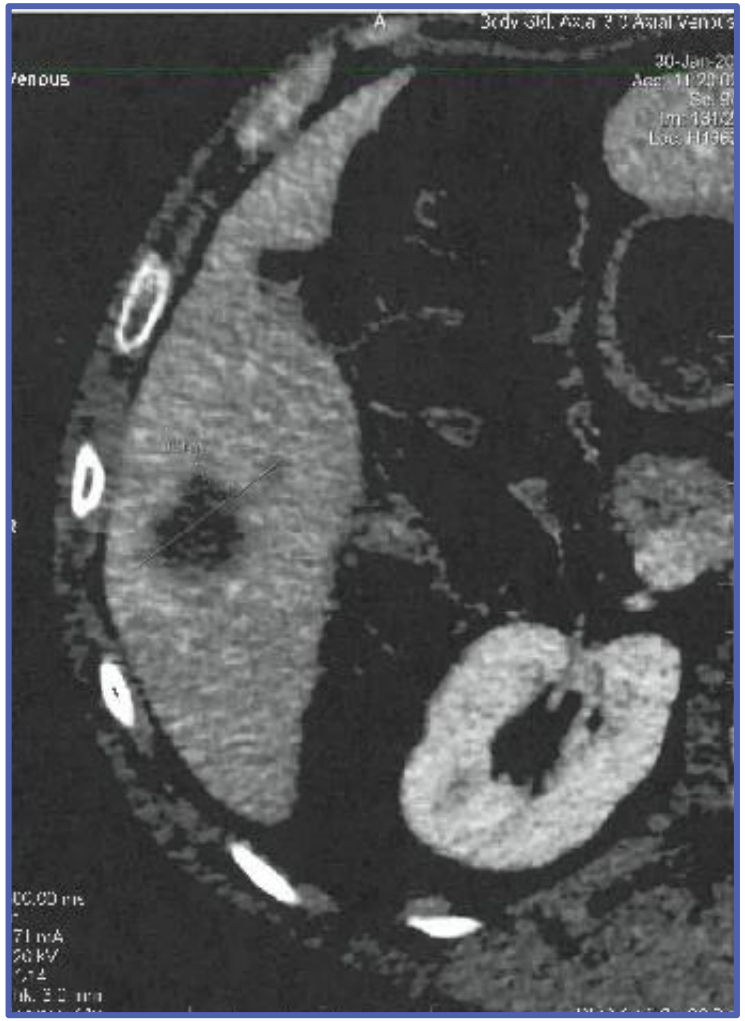
ADP-A2M4 patient with melanoma with high (100% 3+) MAGE-A4 expression

Decrease in target lesion (-40% max. change in 6 cm SLD) with progressive disease (PD) due to new lesions

Baseline



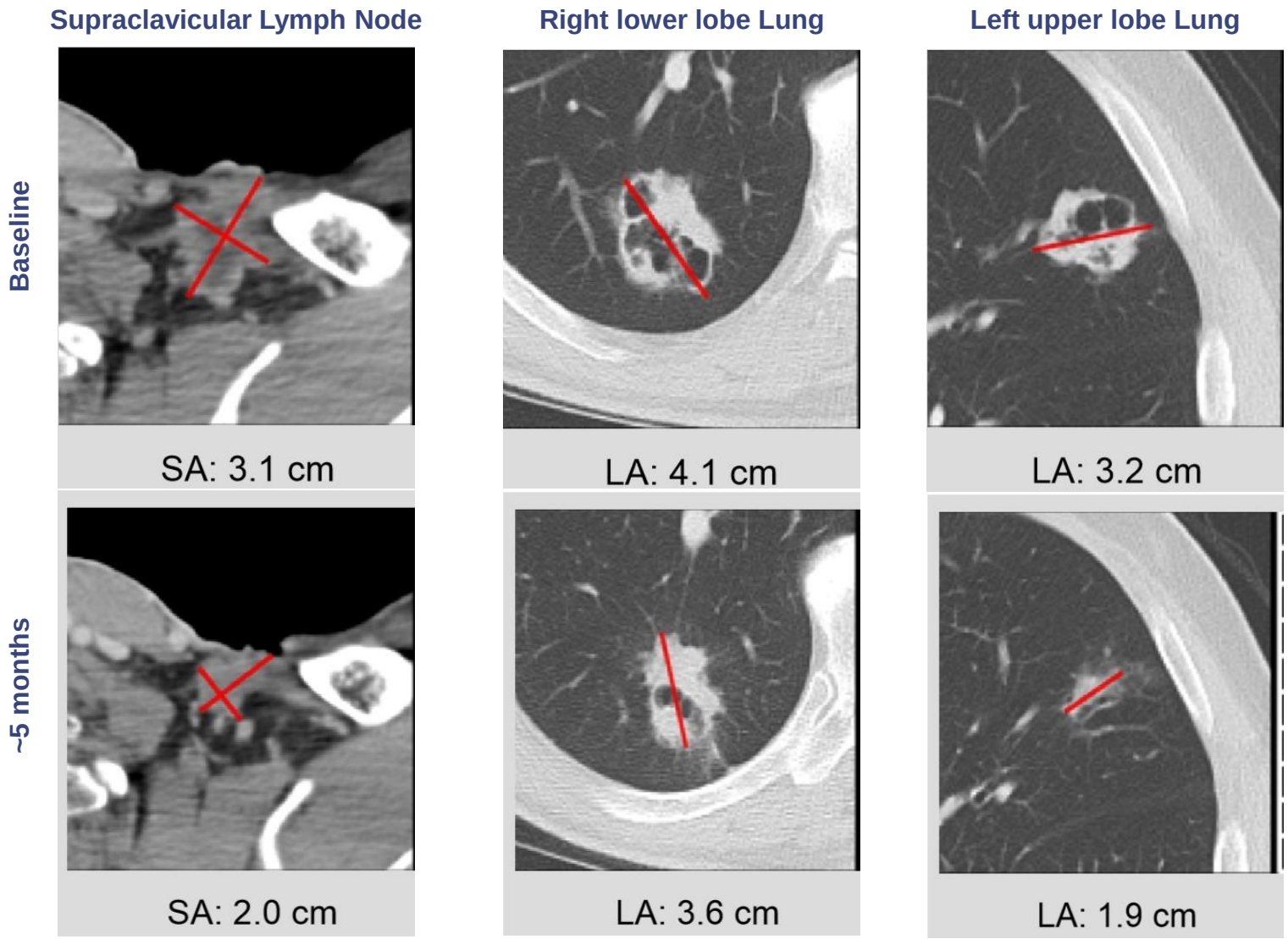
Week 10



Patient had a -40% maximum change in SLD; best overall response is PD due to new lesions
Data cut off 30 April 2019 (as reported on 06 May 2019)

ADP-A2M10 patient with NSCLC with high (90% 3+) MAGE-A10 expression

Stable disease with decrease in target lesion and disappearance of non-target lesion



Patient received second infusion at Week 16; post-baseline scans presented are after second infusion; first infusion 6B, second was 5.2B
Data cut off 26 Apr 2019 (as reported on 06 May 2019)

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Transforming activity into durable responses

Improving SPEAR T-cell activity for cancer patients

Translational Learnings

- ✓ 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
- ✓ Engage wider immune system
- ✓ New targets in development

New Studies

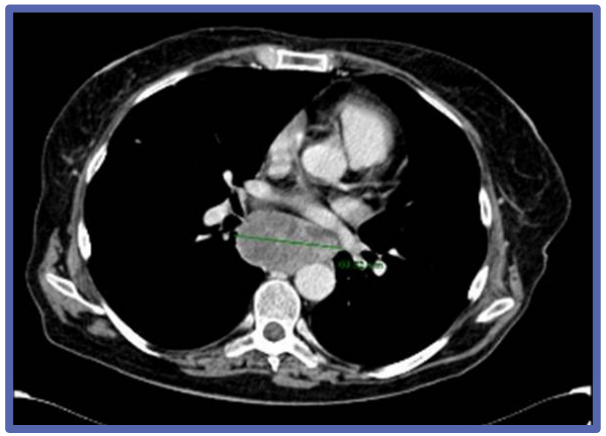
- ✓ ADP-A2M4CD8 next-generation SURPASS trial
- ✓ ADP-A2M4 low radiation sub-study at MD Anderson Cancer Center

Combination with PD-1 inhibitor

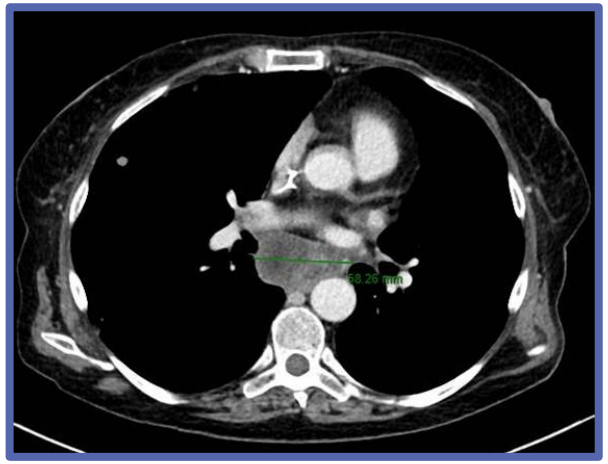
ADP-A2AFP now dosing in Cohort 3 at target doses of 5 billion transduced SPEAR T-cells

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

Baseline

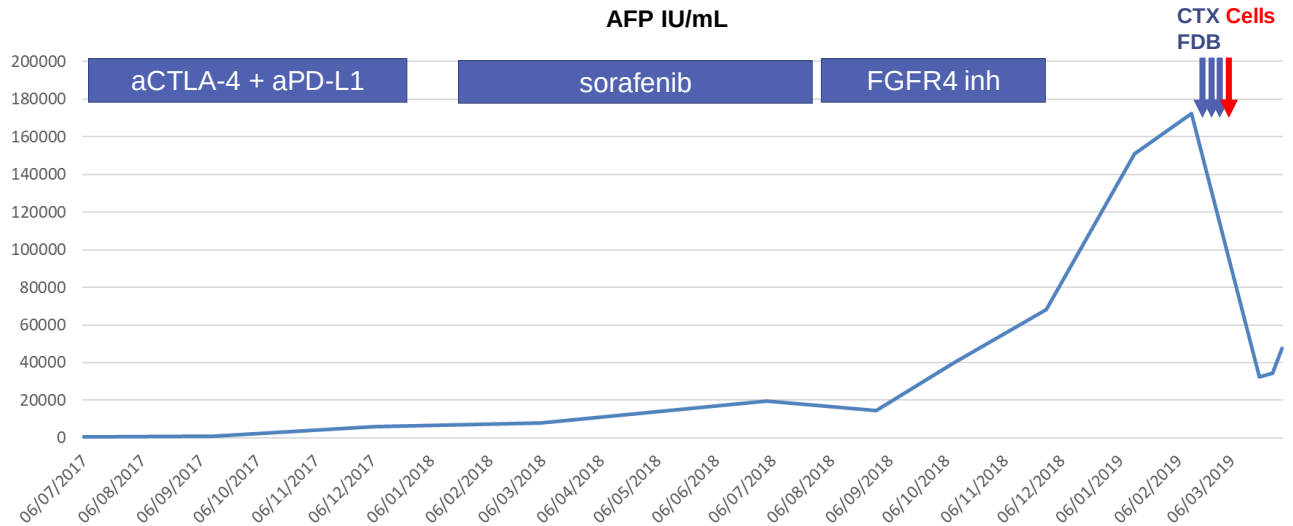


Week 4



Up to 20 patients in ADP-A2AFP trial

Cohort 1 ✓	Cohort 2 ✓	Cohort 3 (Dosing)	Expansion Phase
100m cell dose target	1B cell dose target	5B cell dose target	Up to 10B cells
Complete	Complete	In progress	Not started
21-day stagger	7-day stagger	7-day stagger	No stagger
(Cy: 500 mg/m^2/d) x 3d; (Flu: 20 mg/m^2/d) x 3d	(Cy: 500 mg/m^2/d) x 3d; (Flu: 20 mg/m^2/d) x 3d	(Cy: 600 mg/m^2/d) x 3d; (Flu: 30 mg/m^2/d) x 4d	(Cy: 600 mg/m^2/d) x 3d; (Flu: 30 mg/m^2/d) x 4d



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Beyond our current therapies in clinical trials

Our allogeneic program as well as partnerships for next-gen cell therapies

Our allogeneic program

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

- Significant progress with stem-cell-derived T-cells
- Produce T-cells from stem cells that respond to cancer targets*
- Can be used with any engineered T-cell (TCR and CAR-T)
- Process does not use human serum or stromal cell lines
- Enables scale-up, GMP manufacture of edited off-the-shelf lines

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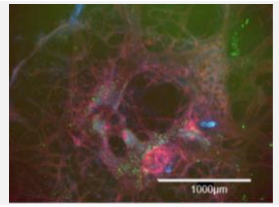

CD34 (red) CD3 (green) nuclei (blue)

Partnerships for next-generation therapies

Noile-Immune Biotech

Proliferation inducing and migration enhancing (PRIME) technology

- Next-gen cells would secrete cytokines IL-7 and CCL19
- Improve proliferation / trafficking of SPEAR T-cells & patient's own T-cells into tumors

ALPINEImmuneSciences

Secreted & transmembrane immunomodulatory proteins (SIP™ and TIP™)

- Engage further rapid and flexible immunomodulatory mechanisms
- Enable the development of next-gen SPEAR T-cells with enhanced antitumor potential

* ASGCT 2019

Looking forward

Data from all programs over next 12 months

2H 2019

SPEARHEAD-1 trial started ✓
SURPASS trial started ✓
Radiation sub-study started ✓
Dosing in Cohort 3 ADP-A2AFP ✓
ADP-A2M10 trials conclude enrollment
ADP-A2M4 Phase 1 trial continues

1H 2020

Durability of sarcoma responses
ADP-A2AFP data update
Safety and response data from SURPASS trial
SPEARHEAD-1 interim futility
ADP-A2M4 Phase 1 trial continues

Beyond 1H 2020

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

Financial Guidance

Funded through Q3 2020

Total liquidity of $102.9 million*

Funded through Q3 2020

* As of 06 Nov 2019 - Total Liquidity (a non-GAAP financial measure) is the total of cash and cash equivalents and marketable securities, which is explained and reconciled to the most directly comparable financial measures prepared in accordance with GAAP.


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November / December 2019

Additional information

Started Phase 2 SPEARHEAD-1 trial

Well-positioned to execute based on years of engagement with sarcoma community

Single-arm, Phase 2 trial in more than 20 centers (North America & EU)

Sample size of 60 patients

- Advanced (metastatic or inoperable) synovial sarcoma or MRCLS, who have received prior chemotherapy
- HLA-A*02 & MAGE-A4 antigen positive
- MAGE-A4 expression 30% (2^+, 3^+)

Primary endpoint

- Overall Response Rate by RECIST v1.1 by independent review
- Interim futility: 3^+ responses in first 15 patients for trial continuation (1H/2020)

Safety endpoints with Independent Data Safety Monitoring Board

Exploratory endpoints: translational and patient-reported outcomes

Treatment

- Lymphodepletion: (Cy: 600 mg/m^2/d) x 3d; (Flu: 30 mg/m^2/d) x 4d
- Dose: up to 10 billion transduced SPEAR T-cells

United States Orphan Drug Designation for Treatment of Soft Tissue Sarcomas Granted to ADP-A2M4

Started Phase 1 SURPASS trial (ADP-A2M4CD8) first next-gen SPEAR T-cell in clinic

Focused on converting antitumor activity into clinical responses

Single-arm, Phase 1 trial (North America & EU)

Sample size up to 30 patients

- Advanced (metastatic or inoperable) cancer (Bladder, Melanoma, Head & Neck, Ovarian, NSCLC, Esophageal, Gastric, Synovial sarcoma, MRCLS)
- HLA-A*02 & MAGE-A4 antigen positive
- MAGE-A4 expression 30% (2^+, 3^+)

Endpoints

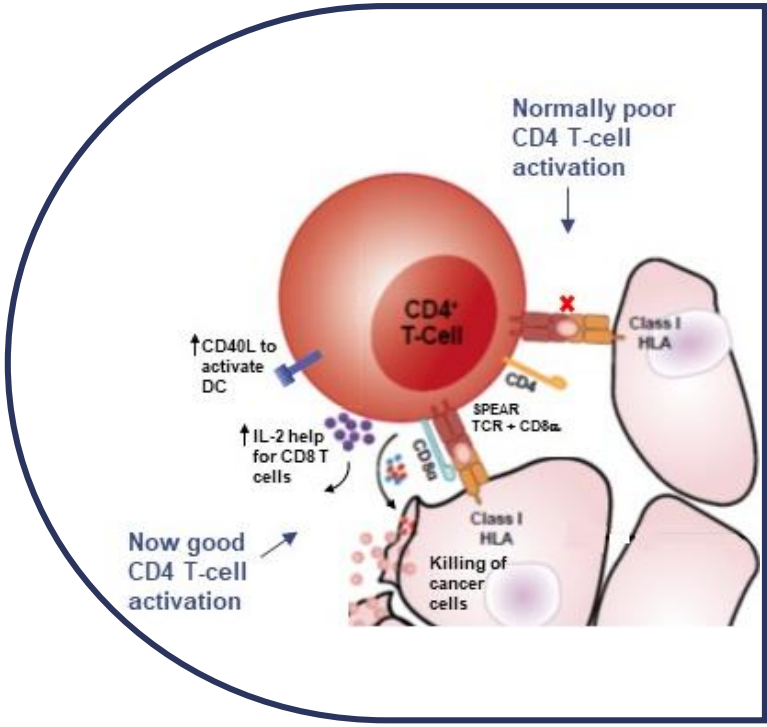
- Safety and tolerability
- Secondary endpoint of antitumor activity

Dose escalation 3 cohorts of 3 patients each; expand to 6 if DLTs

Shorter stagger (14 days) between patients – anticipate faster dose escalation

Treatment

- Lymphodepletion: (Cy: 600 mg/m^2/d) x 3d; (Flu: 30 mg/m^2/d) x 4d
- Cohort 1 (0.8 to 1.2B cells)
- Cohort 2 (1.2 to 3.0B cells)
- Cohort 3 (3.0 to 6.0B cells)
- Expansion phase up to 10B cells



To increase potency of CD4$^+$ T-cells, a CD8α co-receptor is expressed alongside the engineered TCR to increase TCR binding avidity and enhance polyfunctional response of engineered CD4$^+$ SPEAR T-cells to MAGE-A4 target

Preclinical data at AACR 2019 – no evidence of off-target reactivity, improved cytokine release by DCs and T-cells in culture with MAGE-A4$^+$ cells, improved killing of MAGE-A4 target cells by CD4+ SPEAR T-cells expressing CD8 (virtually no killing by CD4$^+$ cells without CD8 element)

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

Focused on converting antitumor activity into clinical responses

Sub-study of the ADP-A2M4 Phase 1 trial at MD Anderson Cancer Center

Sample size up to 10 patients

- Advanced (metastatic or inoperable) cancer (Bladder, Melanoma, Head & Neck, Ovarian, NSCLC, Esophageal, Gastric, Synovial sarcoma, MRCLS)
- HLA-A*02 & MAGE-A4 antigen positive

Endpoints

- Safety and tolerability
- Secondary endpoint of antitumor activity

Treatment

- 7Gy (low dose) per lesion or isocenter
- Maximum of 5 lesions or isocenters
- Administered prior to lymphodepletion
- Lymphodepletion: (Cy: 600 mg/m^2/d) x 3d; (Flu: 30 mg/m^2/d) x 4d
- Up to 10B cells

Preclinical data shows low dose radiation may improve T-cell penetration into tumors *

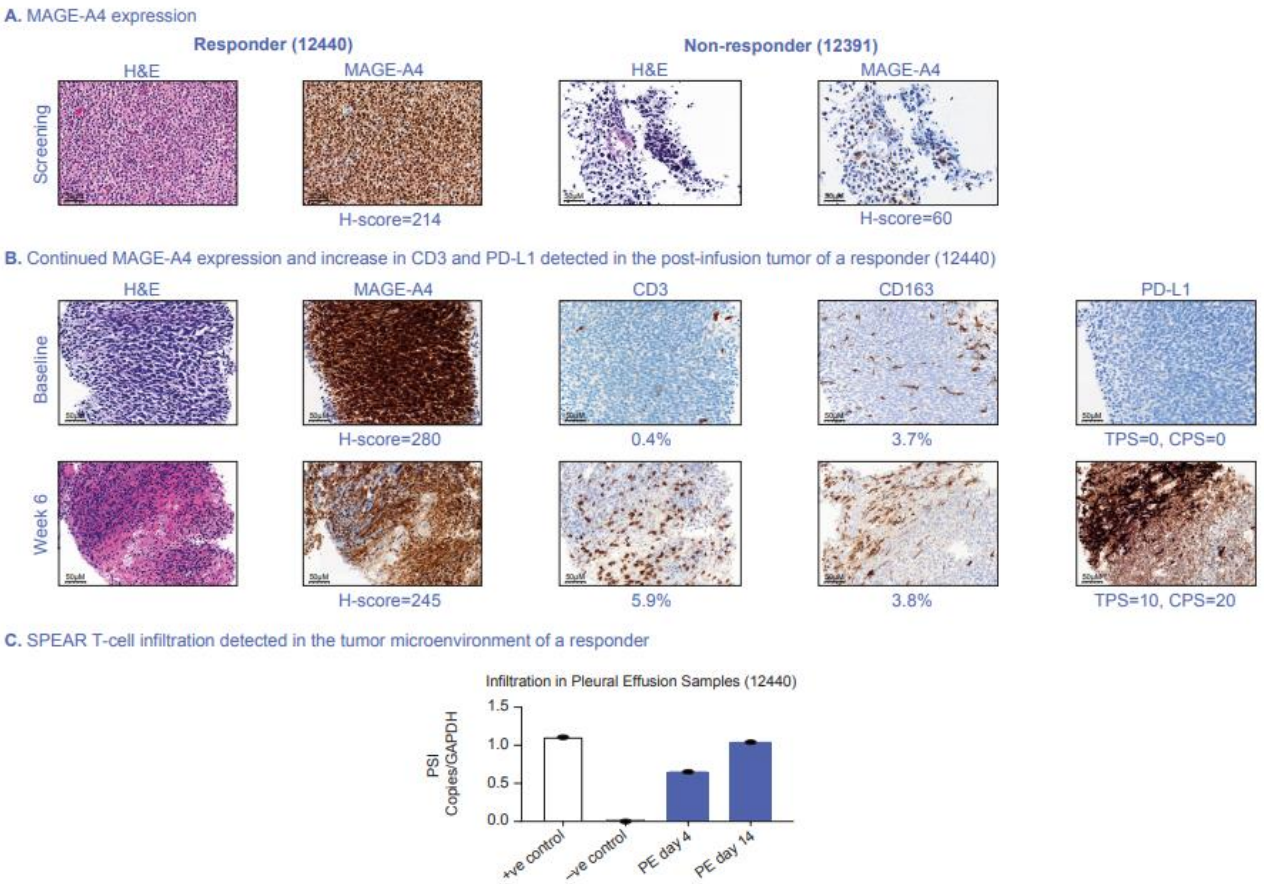
* Barsoumian, 2018; DeSelm, 2018

SITC case studies 2019

Responder vs. non-responder synovial sarcoma patients in ADP-A2M4 Phase 1 trial

- High antigen expression levels, IL-15 and IFNγ cytokine induction, good engraftment, tumor site trafficking, and cytolytic function of SPEAR T-cells may be associated with favorable responses in synovial sarcoma patients treated with ADP-A2M4
- PD-L1 upregulation in response to SPEAR T-cell tumor infiltration and activity may represent a mechanism of resistance
- We continue to analyze biomarkers in the 10 additional synovial sarcoma patients who have been treated

Figure 3. Intra-tumoral infiltration of SPEAR T-cells post-infusion without loss of antigen expression in a responder



A. IHC for MAGE-A4 was performed on enrollment (archival) pre-infusion FFPE biopsies taken from example responder and non-responder patients **B.** IHC for MAGE-A4 and immune markers was performed on FFPE tumor biopsies collected from the responder patient at the pre-infusion baseline visit and at early on-treatment following infusion. H-score = (1 × % tumor stained at 1+ intensity) + (2 × % tumor stained at 2+ intensity) + (3 × % tumor stained at 3+ intensity). CPS and TPS scoring for PD-L1 expression was performed as recommended by the manufacturer of the PD-L1 IHC 22C3 pharmDx assay in an RUO setting **C.** A digital PCR-based assay was performed on DNA extracted from frozen cells isolated from the patient's PE fluid to detect the lentiviral vector PSI sequence and GAPDH

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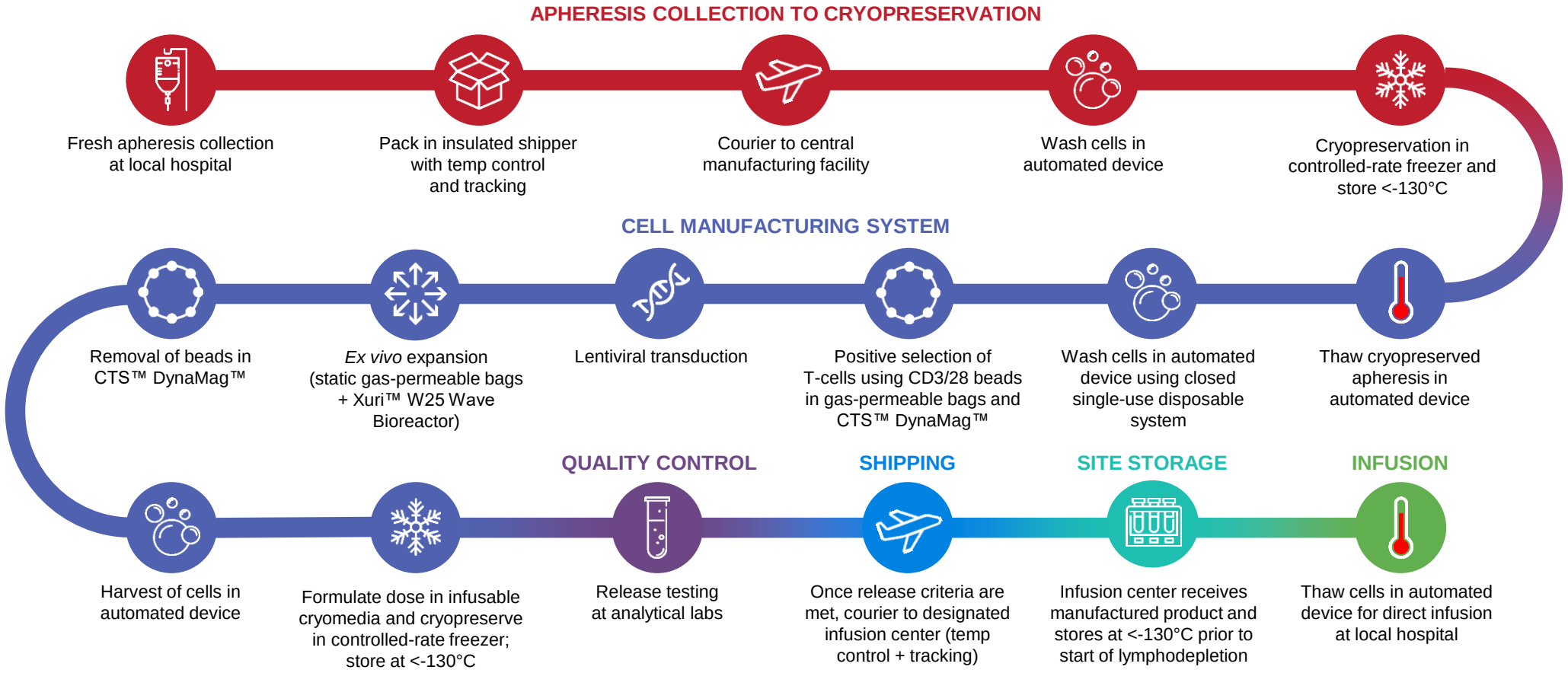
The Patient Cell Journey



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