# SPEAR-heading



Corporate Deck
June 2021

## 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-Q filed with the Securities and Exchange Commission (SEC) on May 6, 2021 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.



## Our vision and mission – Arming cell therapies to target solid tumors

Arming Cells.
Against Cancer.
For Good.

To transform the lives of people with cancer by designing and delivering cell therapies





## 5-year core value drivers: our "2-2-5-2" plan



## Two marketed SPEAR T-cell products targeting MAGE-A4

- Synovial sarcoma and MRCLS
- Esophageal and EGJ cancers



## TWO additional BLAs for SPEAR T-cell products

- Additional indications for MAGE-A4 targeted products
- ADP-A2AFP



## Five autologous products in the clinic

- HiT
- Next-gen TILs
- New targets
- Broader HLA coverage



## TWO allogeneic products entering the clinic

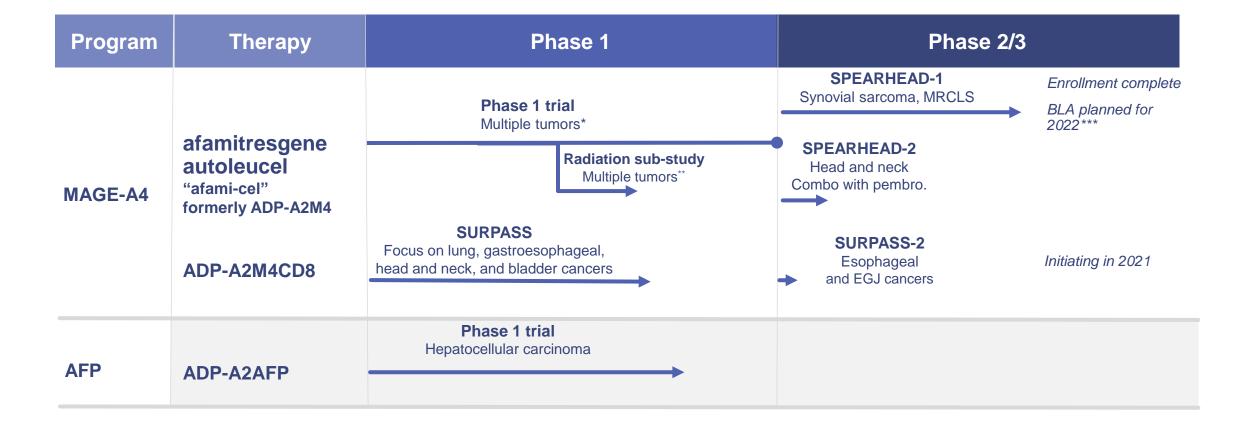
- SPEAR T-cell product targeting MAGE-A4
- HiT mesothelin partnered with Astellas

**Integrated Cell Therapy Capabilities** 

Research | Preclinical | Translational | Clinical | CMC | Regulatory | Commercial



## A strong autologous clinical pipeline in multiple clinical trials in 10 solid tumors Goal to launch first TCR T-cell therapy in 2022



<sup>\*</sup> Bladder, Melanoma, Head and Neck, Ovarian, Non-small cell lung cancer (NSCLC), Esophageal, Gastric, Synovial sarcoma, MRCLS

<sup>\*\*</sup> Site specific protocol amendment with MD Anderson Cancer Center

<sup>\*\*\*</sup>Planned for synovial sarcoma

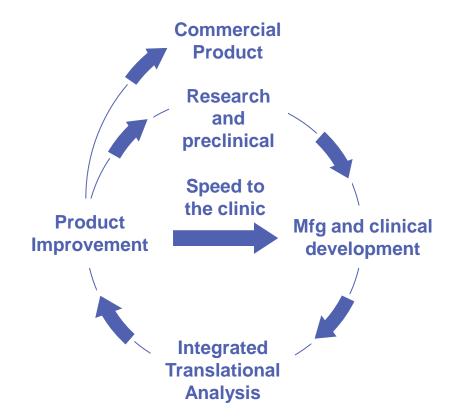
## Strong pipeline to deliver five products to the clinic by 2025

Aiming for curative and mainstream therapies

Platform	Product	Discovery	Preclinical
Autologous SPEAR T-cells	ADP-A2AFP+CD8 next-gen		
	MAGE-A4 next-gen approaches (IL-7, IL-15, dnTGFbeta, PDE7)		
	IL-7/CCL19 Noile-Immune Biotech		
	Undisclosed ALPINEImmuneSciences		
	HLA-A1 MAGE-A4		
	HLA-A24 MAGE-A4		
	HLA-A24 AFP		
	PRAME gsk		
TILs	TIL IL-7		
HiTs	HiT targets (e.g., GPC3)		
Allogeneic	HiT mesothelin astellas		
	Allogeneic T-cells targeting MAGE-A4		



## Integrated capabilities delivering value across the pipeline



## **Examples of value creation**

- SPEARHEAD-1 enrollment completed in ~12 months
- ADP-A2M4CD8 IND to registration directed trial ~2 years
- Security of vector supply and >90% reduction in costs
- Manufacturing innovation drives ~40% reduction in SPEAR T-cell therapy COGs

## **Integrated Cell Therapy Capabilities**

Research | Preclinical | Translational | Clinical | CMC | Regulatory | Commercial



## Planned data updates and catalysts for 2021 and 2022

Funded into 2023

## 2021

- √ SPEARHEAD-1 preliminary data at ASCO
- Initiate SURPASS-2 trial with ADP-A2M4CD8 in esophageal and EGJ cancers
- SURPASS data update at ESMO
- ADP-A2AFP Phase 1 trial data update at ILCA
- Radiation sub-study data update\*
- Update on additional translational data at SITC
- SPEARHEAD-1 full data update at CTOS



## Two

marketed SPEAR T-cell products targeting MAGE-A4

## Two

additional BLAs for SPEAR T-cell products

## **Five**

autologous products in the clinic

## Two

allogeneic products entering the clinic

## 2022

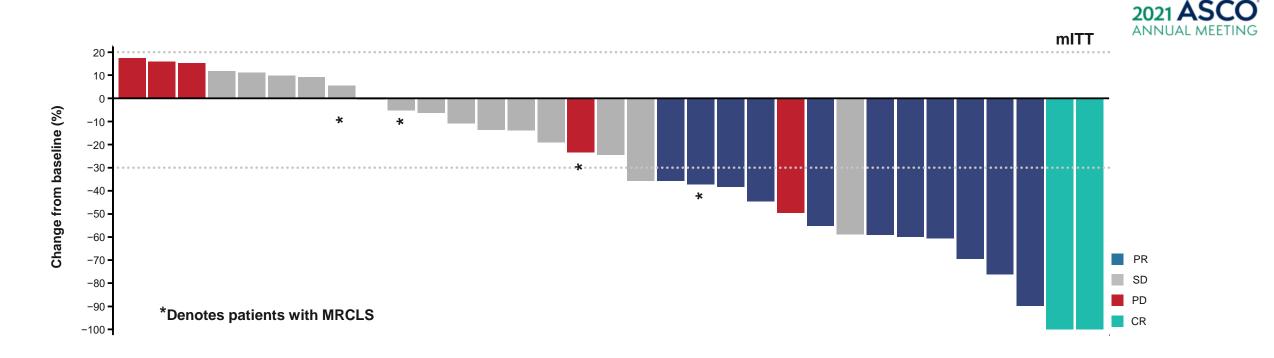
- File BLA and planned launch of afami-cel for people with synovial sarcoma and MRCLS
- Preclinical pipeline program data updates
- Allogeneic platform update
- SPEARHEAD-2 initial clinical data
- SURPASS-2 initial clinical data
- First trial with ADP-TILIL7





## Deep responses observed with afami-cel therapy

Best overall response by RECIST v1.1



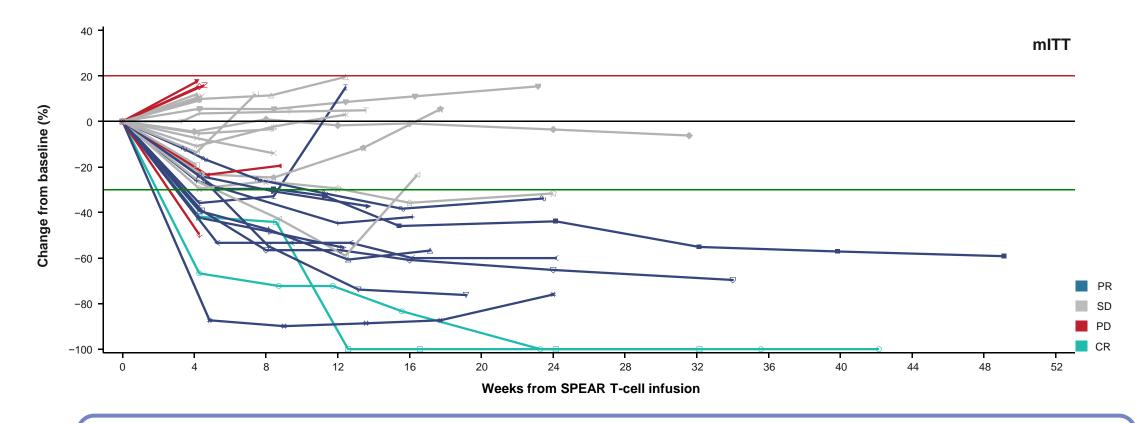
- Overall response rate 39.4% (13/33): synovial sarcoma 41.4% (12/29) and MRCLS 25.0% (1/4)
- Two CRs in patients with synovial sarcoma
- Disease control rate of 84.8% (28/33)

CR = complete response; mITT = modified intent to treat; MRCLS = myxoid/round cell liposarcoma; PD = progressive disease; PR = partial response; SD = stable disease; Data represent percent changes from baseline in sum of diameters (sum of the long diameters for non-nodal lesions and short axis for nodal lesions) in target lesions through progression or prior to surgical resection; Reponses evaluated by RECIST v1.1 per Investigator assessment; Data excludes 4 patients who were pending 1st efficacy assessment as of the data cut-off

Data cut-off March 29, 2021



## Initial durability encouraging with afami-cel therapy Best overall response by RECIST v1.1



- Improvements in sum of diameters over time have been observed
- Median duration of response not reached range (weeks): 4.3+, 38.0+



CR = complete response; mITT = modified intent to treat; PD = progressive disease; PR = partial response; SD = stable disease; Data represent percent changes from baseline in sum of diameters (sum of the long diameters for non-nodal lesions and short axis for nodal lesions) in target lesions through progression or prior to surgical resection; Reponses evaluated by RECIST v1.1 per Investigator assessment; + Denotes censored ongoing response

Data cut-off March 29, 2021



## There is a large unmet medical need for people with synovial sarcoma



"Initial data from SPEARHEAD-1 indicate that afamicel has the potential to offer people with synovial sarcoma a promising new treatment option where there is currently a great unmet medical need. As clinicians, we want to be able to provide a treatment regimen that can help offer a better quality of life."

-- Dr. Sandra P. D'Angelo of the Memorial Sloan Kettering Cancer Center



"Amongst the limitations of using chemotherapy to treat synovial sarcoma is the need to always be on a therapy and to deal with the side effects that come from it. Chemo patients are not able to live a normal life. What we're really looking for is a therapy where once it's performed, it's durable and you don't need another one."

 Dr. Brian Van Tine, Associate Professor of Medicine, Division of Oncology, Section of Medical Oncology, Washington University School of Medicine



"After suffering from misdiagnosis or years-long journey to diagnosis, people living with synovial sarcoma struggle with limited, and often ineffective, treatment options. A treatment for synovial sarcoma patients that gives them more options, a better prognosis, and a better quality of life is long overdue."

-- Brandi Felser, CEO, Sarcoma Foundation of America



## SPEARHEAD-1 data will be used to support marketing application next year for afami-cel First milestone in our 2-2-5-2 strategic plan

- Afami-cel response rates compare favorably to available 2nd line therapies\*
- SPEARHEAD-1 is ongoing
  - Cohort 1 (n=45) enrollment and treatment is complete, and Cohort 2 (n=45) is currently recruiting
  - The primary evidence supporting marketing applications will be based on Cohort 1
- BLA filing on track for 2022 for people with synovial sarcoma and MRCLS
- Planning for successful marketing applications and regulatory agency interactions

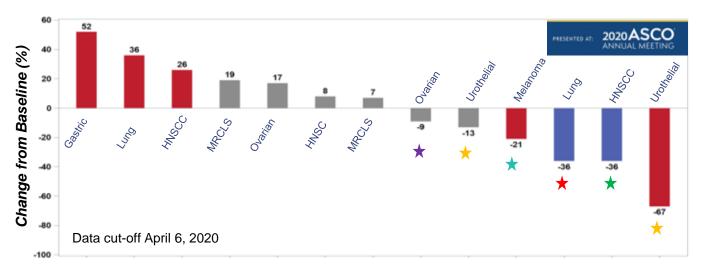




## The power of SPEAR T-cells targeting MAGE-A4 in multiple tumor types

The basis for new Phase 2 trials and future BLAs

## Afamitresgene autoleucel Phase 1 trial best overall response (BOR) in 13 patients with multiple tumor indications\*

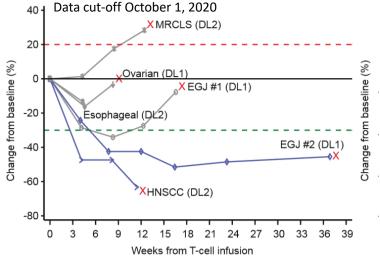




- ★ Esophagogastric Junction (EGJ)
- ★ Head and Neck
- **★** Lung

## Other reductions in tumor size: ★ Esophageal ★ Urothelial (Bladder) ★ Ovarian ★ Melanoma

# ADP-A2M4CD8 SURPASS Trial BOR in 6 patients with multiple tumor indications Data cut-off October 1, 2020 1.3514 -13.37 -16.13 \*\* PR SD PD -60 -80 -63.16





## Marked improvement in a patient with EGJ cancer treated with ADP-A2M4CD8

Single dose of 1.2 billion transduced cells with over 9 months until progression

lymph node

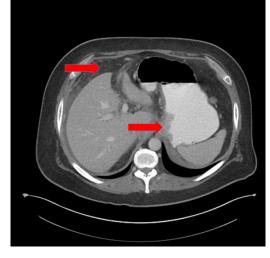
Baseline





Ascites + Peritoneal thickening

Periportal





31-yr-old male with Stage IV EGJ cancer, HER2neg **Diagnosed July 2018** 

## **PRIOR THERAPY**

- FLOT

Chemotherapy (2018-2019)

- Atezo with BL-8040

- FOLFIRI

Ramucirumab and paclitaxel (bridging)

Radiation

- 30 Gy to abdomen/retroperitoneal lymph node

## ADP-A2M4CD8

High MAGE-A4 expression (100% 3+)

1.2 billion SPEAR T-cells: 30-Oct-2019

Typical adverse events

### **RESPONSE**

Partial Response with 51.52% reduction in target lesions

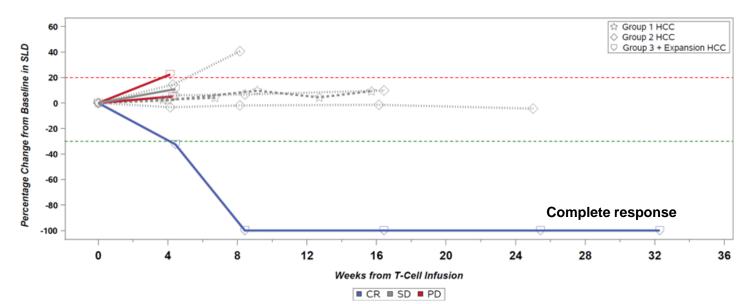
Marked symptomatic improvement - reduced narcotic requirement for pain, resolution of ascites, general well-being

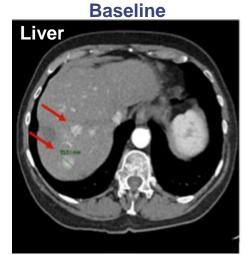
Disease progression ~8.5 months after receiving SPEAR T-cells



## Complete response in the Phase 1 trial demonstrates potential of ADP-A2AFP

Trial ongoing in expansion phase







Best overall response	Group 1 (n=2)	Group 2 (n=3)	Group 3 and expansion (n=4)
Complete response	0	0	1 (25%)
Stable disease	2 (100%)	3 (100%)	1 (25%)
Progressive disease	0	0	2 (50%)





## Large market opportunity potential with SPEAR T-cells targeting MAGE-A4

When considering all indications in our trials there is a large potential patient population eligible for treatment

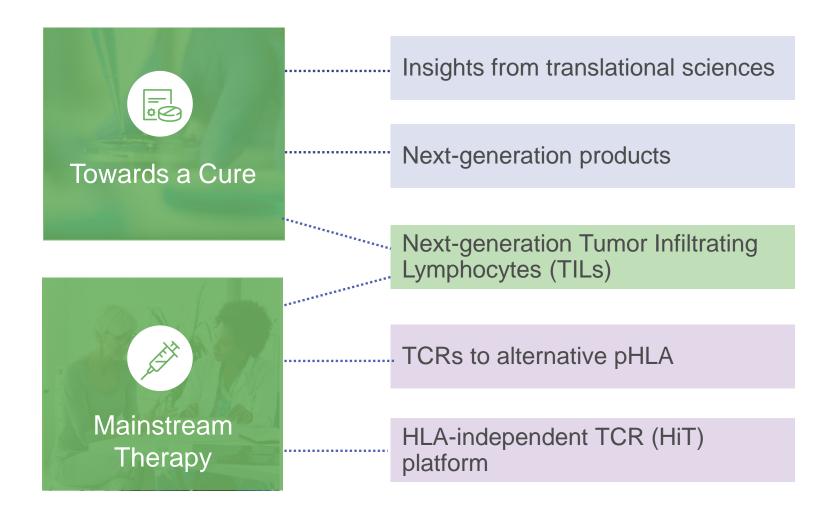
Indication	Mortality US and EU*	MAGE-A4 Expression **	Potential MAGE-A4 +ve Patients	Potential MAGE-A4 +ve Patients Factored for HLA***
Synovial sarcoma	1,804+	67 %	1,209	496
Myxoid/round cell liposarcoma	2,000	34 %	680	279
Gastroesophageal (esophageal, EGJ, and gastric)	101,080	17 %	17,184	7,045
Head and neck	44,500	18 %	8,010	3,284
Urothelial	53,180	33 %	17,549	7,195
NSCLC (squamous)	101,661	38 %	38,631	15,839
Melanoma	19,750	16 %	3,160	1,296
Ovarian	38,840	22 %	8,545	3,503
			Total MAGE-A4: 94,968	Total MAGE-A4 HLA-A*02: 38,937





## Strong pipeline to deliver five products to enter the clinic by 2025

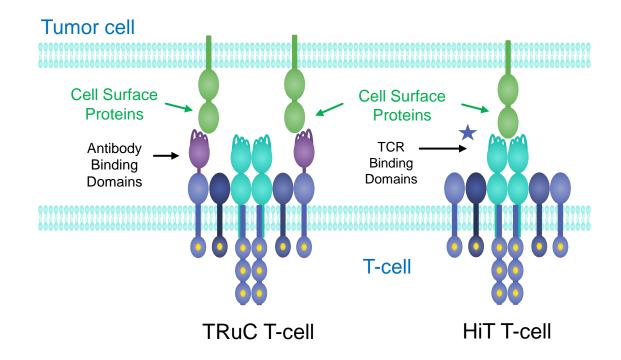
Aiming for curative and mainstream therapies



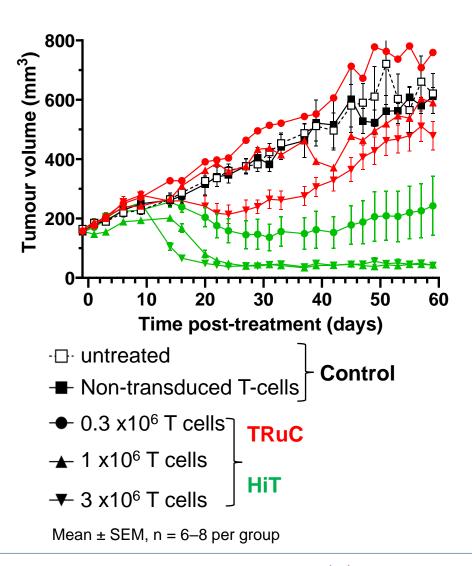


## HiT induces strong, dose-dependent and persistent tumor regression in vivo

HiT outperformed TRuC in a mouse tumor model



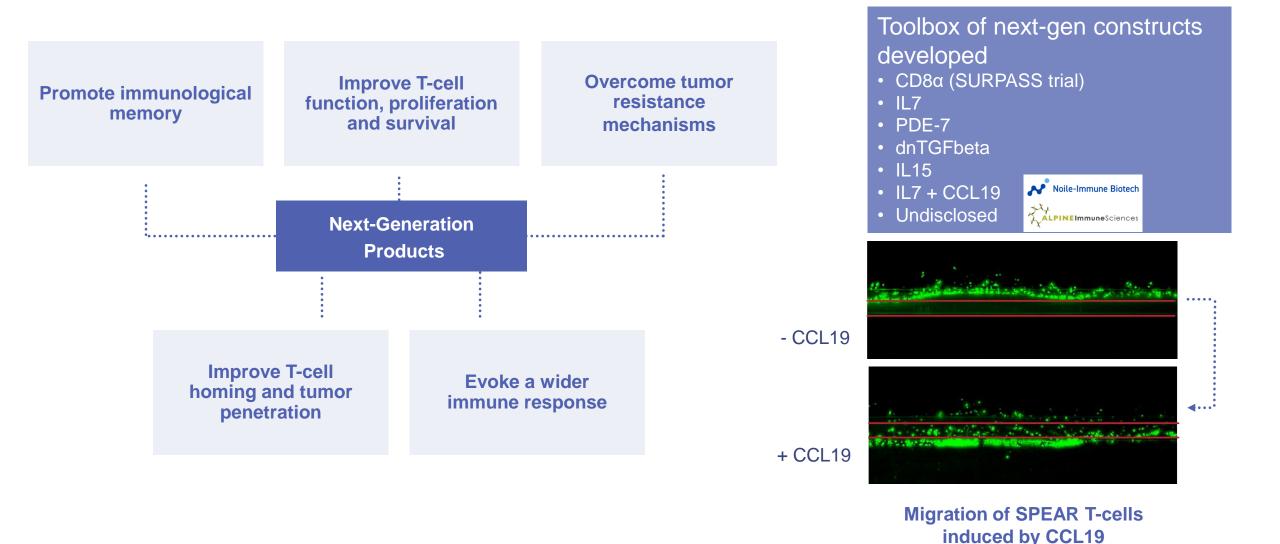






## Enhancing SPEAR T-cells to improve patient response, survival, and quality of life

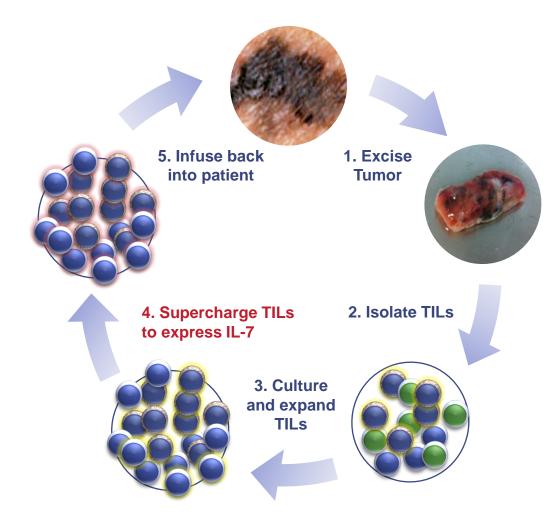
Next-generation products





## Working with CCIT to develop next-generation 'supercharged' TILs co-expressing IL-7

The future of melanoma treatment?



## Partnership with leading TIL therapy center (CCIT, Denmark) led by Inge-Marie Svane



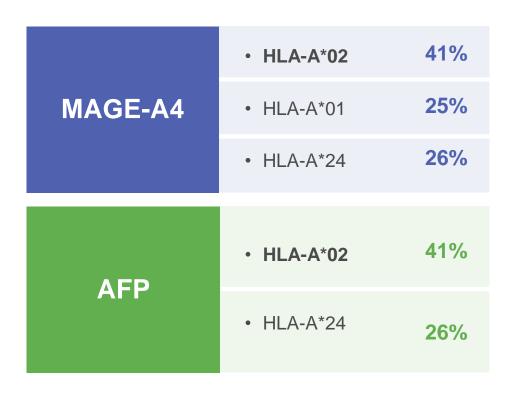
- Tumor Infiltrating Lymphocytes (TILs) therapy is efficacious in solid tumors, including melanoma
- Aim to transform patient responses with a nextgeneration TIL product
  - TIL-IL7 product progressing to the clinic
- Builds on our strengths in TCR discovery, nextgeneration product development and manufacturing
- Broad market potential

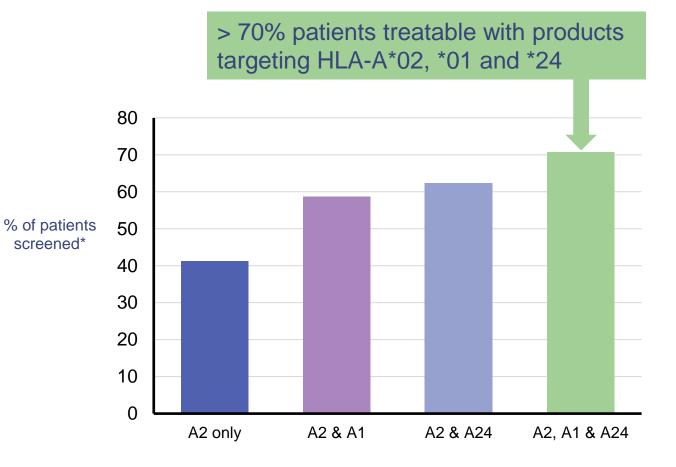


## Increase treatable patient population with products targeting additional HLA types

Towards mainstream therapy

## Single HLA allele frequency in patients









## Gene edited stem cells provide a flexible platform while minimizing batch to batch variation

Potential to build a broad family of future products across multiple cell types



- Single donor cord blood
- High proliferative potential
- Reproducible starting material

- Overcomes lentivector capacity limit
- Flexibility to add multiple next-gens

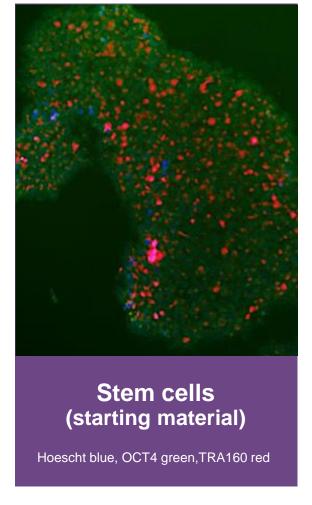
- Single cell line for characterization
- Defined media composition
- No serum or feeder lines

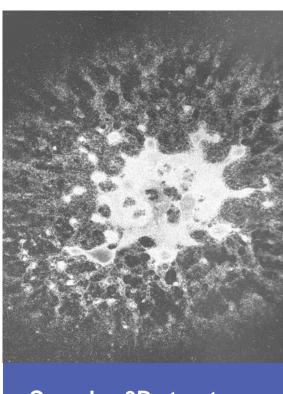
**Greater Control** 



## Differentiation process mimics early T-cell development in a dish

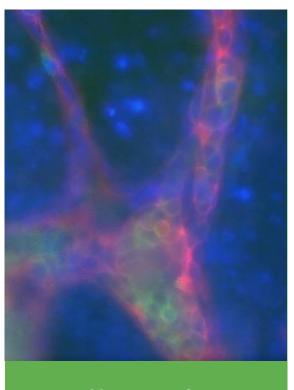
Hematopoietic organoids generate T-cell progenitors that mature to form iT-cells





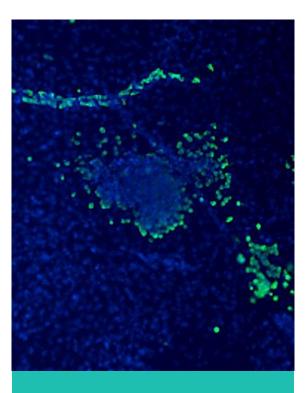
Complex 3D structures self assemble

Brightfield



Hemogenic endothelium forms

Hoescht blue, CD45 green, CD34 red



**T-cells form** 

Hoescht blue, CD3 green

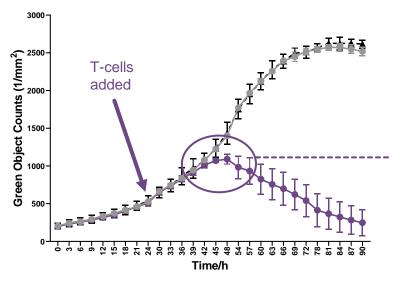


## Our allogeneic iT-cells kill MAGE-A4 expressing target cells

Stem cell derived allogeneic iT-cells kill faster than first-generation autologous SPEAR T-cells

**Autologous T-cells** 

transduced with ADP-A2M4 lentivirus

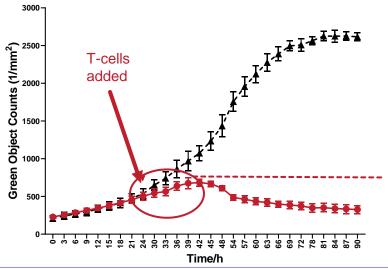


Non-transduced autologous T-cells have no effect on tumor line growth

Autologous ADP-A2M4 SPEAR T-cells kill targets 18-24hr after addition

Allogeneic iT-cells

edited to express the same SPEAR TCR targeting MAGE-A4



Tumor line growth curve (no T-cells added)

Allogeneic iT-cells start killing targets 6-9hr after addition





## Leading capabilities for designing and delivering cell therapies

Integrated, internal capabilities are the foundation for long-term value creation



## **Philadelphia**

- Autologous product manufacturing
- Clinical Development
- Commercial
- Corporate

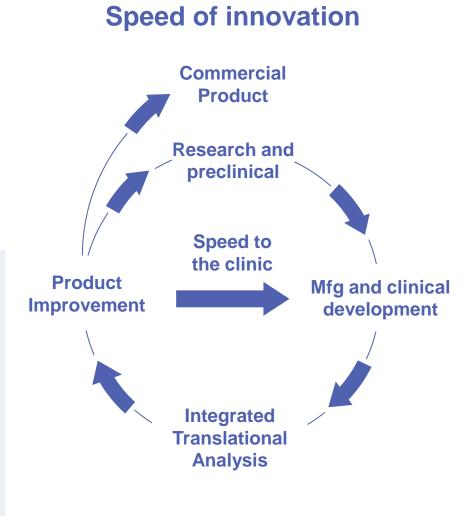
## **Milton Park**

- Pipeline Research
- Allogeneic research
- Process and analytical development
- Corporate



## Stevenage

 GMP Lentiviral vector manufacturing





## Current total liquidity at end of Q1 2021 was ~\$318M\*

Well financed and ready to execute on broad range of opportunities/value drivers



# SPEAR-heading



Corporate Deck June 2021