NOVEL TARGETED CANCER IMMUNOTHERAPIES MADE IN TEXAS

CPRIT’s Product Development Research Showcase
November 13, 2017

Harpreet Singh, PhD, President & CEO, Immatics US Inc.
World-leading XPRESIDENT® Target and TCR discovery engine enabling
- Development of autologous and allogeneic adoptive cell therapies (ACT)
- Development of TCR Bispecifics

Joint Venture with MD Anderson Cancer Center for ACT development
Two clinical studies started in 2017
Co-funded by CPRIT Product Development Grant (up to $19.7m)

Corporate Background
- Major corporate partnerships with Roche and Amgen
- Joint venture in Houston, TX (Immatics US Inc.) with MD Anderson to clinically develop ACT
- Raised > $230m in financing since founding
- $58m financing in 2H2017

Leadership Immatics US
Pres. & CEO  Harpreet Singh
CSO           Steffen Walter
CTO           Toni Weinschenk
CMO           Carsten Reinhardt
CBO           Rainer Kramer

Staff 45 FTEs Houston (90 FTEs Germany)
Cancer Immunotherapy: A New Era

The game changers

1. **Checkpoint inhibitors**
   → “releasing the brakes“ from immune cells embedded in melanoma cancer tissue

2. **Adoptive cellular therapy (ACT)**
   → gene therapy of immune cells to target acute lymphoblastic leukemia
Cancer Immunotherapy: A New Era

News flow in the last months in adoptive cell therapies:

• FDA approval for CD19 CAR-T by Novartis
• Clinical efficacy established for BCMA CAR-T in multiple myeloma pts shown by Bluebird Bio and Nanjing Legend at ASCO 2017
• Promising clinical efficacy indicated for MAGE-A3 TCR-T in metastatic pts shown by NCI/ Kite Pharma at AACR 2017
• Acquisition of Kite Pharma by Gilead for $11.9b
• GSK exercises option for Adaptimmune NY-ESO1 TCR-T for $61m
• FDA approval for CD19 CAR-T by Kite Pharma/Gilead
• Juno publishes a 80% overall response rate at 3 months for DLBLC patients at ASH 2017
The Problem: The Missing Targets

Current immunotherapies are limited to liquid cancers and subpopulations of solid cancers with high mutation rate.

The medical need for all other cancer types is largely unmet.
The solution: accessing the intracellular target space

- The number of surface protein targets accessible to mAb and CAR-T approaches is limited
- There are 3-4 times more intracellular targets than surface protein targets
- The T-cell receptor allows access to the intracellular target space via HLA-peptide presentation – the target space discovered and defined by Immatics’ founders
- HLA-peptide targets by TCR-based approaches (TCR Bispecifics and TCR-based ACT) are the only way to efficiently target solid tumors with low mutational burden – the largest part of the cancer market

Localization of human proteome

- ~75% Plasma membrane (accessible with mAb/CAR)
- ~25% Intracellular or secreted (not accessible with mAb/CAR)

TCR- vs. CAR/mAb-based approach

TCRs can target all cellular proteins through recognition of HLA-presented peptides

2 Uhlen et al., Science 2015
Immatics has built over 10 years a target discovery engine that has yielded hundreds of novel cancer peptide target candidates.

**Primary Cancer tissues**
- AML
- Bladder Cancer
- Breast Cancer
- CLL
- Colorectal Cancer
- Esophagus Cancer
- Gallbladder
- Gastric Cancer
- Glioma
- Liver Cancer
- Melanoma
- Multiple Myeloma
- Non-Hodgkin lymphoma
- NSCLC
- Ovary
- Pancreas Cancer
- Prostate Cancer
- Renal Cell Carcinoma
- SCLC
- Uterus

**Normal Control Tissues**
- Adipose tissue
- Ovary
- Adrenal Gland
- Pancreas
- Artery
- Peripheral nerve
- Bladder
- Pituitary gland
- Blood cells
- Placenta
- Bone Marrow
- Pleura
- Brain
- Prostate
- Breast
- Rectum
- Cartilage
- Salivary gland
- Cervix
- Skin
- Colon
- Small intestine
- Esophagus
- Spleen
- Eye
- Stomach
- Gall bladder
- Testis
- Heart
- Thymus
- Kidney
- Thyroid
- Liver
- Trachea
- Lung
- Ureter
- Lymph node
- Uterus
- Muscle
- Vein

**Immatics XPRESIDENT® Target Database**

- >60 million MS/MS spectra
  - From >10,000 MS experiments
  - From >1,100 tissue samples

- >4,000 tumor-associated candidates
  - filed in patent applications from HIP

- >70 prioritized HLA-A*02 targets
  - covering >20 different tumor types

**XPRESIDENT® delivers**
- **better targets** covering a broad range of cancer types with high unmet medical need
- **safer targets** with higher tumor specificity compared to what is currently developed

Immatics US has an exclusive, perpetual license from Immatics Germany to use all Immatics present and future targets for adoptive cell therapy.
Setup of Immatics US, Inc.

**Strategic Partnership with MD Anderson Cancer Center**

**Complementary expertise are joined in the ACT development of CPRIT funded projects**

- Immatics contributes with i) Target peptides and TCRs  
  ii) Management talent and iii) Funding
- MD Anderson brings i) core expertise in ACT and GMP manufacturing ii) IP and iii) Clinical infrastructure

**Scientific Co-Founders**

Patrick Hwu  
Division Head  
Cancer Medicine

Cassian Yee  
Professor Department of Melanoma Medical Oncology and Immunology  
Director of Solid Tumor Cell Therapy

**Immatics US, Inc.**

- Co-launched 2015 by Immatics Germany and MD Anderson (holds minority position in Immatics US)
- Location: 15,000 sqft facility at Life Science Plaza, Texas Medical Center Campus, Houston, TX
- Setup of a state-of-the-art research and development and GMP manufacturing facilities in Houston
- Currently employing **45 full-time employees** mainly in research, manufacturing and clinical development
Adoptive Cell Therapy (ACT) Development Tracks

**ACTolog®**
- T cells: autologous
- TCR: endogenous
  - HLA/peptide-multimer (fishing rod for T-cell)

**ACTengine®**
- T cells: autologous
- TCR: engineered
  - Retrovirus encoding novel T-cell receptor

**ACTallo®**
- T cells: allogeneic
- TCR: engineered
  - "Off-the-shelf" Gamma-delta T cell encoding novel T-cell receptor

Co-funded by CPRIT
ACTolog® - Concept & Pioneering Work by Prof. Yee

1. Tumor target
   - Biomarker profiling
   - Pre-defined target warehouse

2. T-cell generation process
   - Identification of specific cells
   - Expansion

3. Re-Infusion up to 4 products
   - Multiple products
   - Reduced risk for tumor escape

Clinical Proof of Concept

Prof. Cassian Yee
MD Anderson Cancer Center
Chapuis et al, JCO (2016)

- Early promising clinical efficacy results in metastatic melanoma patients with one target
- 2/10 Patients experienced durable complete remission after infusion of MART1 specific cells generated with the same technology in combination with Ipilimumab

Cancer patient

Images of CT scans showing before and after treatment for metastatic melanoma.
ACTolog® - Progress update

Achievements

1. **8 cancer targets** for ACTolog® target warehouse identified for personalized immunotherapy

2. **GMP T-cell manufacturing process** established to treat patients with up to four different T-cell products

3. Clinical trial designed in refractory/metastatic cancer patients without any established treatment options and high medical need incl. squamous lung cancer, head & neck cancer, ovarian cancer, esophagus cancer

4. Clinical Study approved by FDA

5. **Trial started** in July 2017 at MD Anderson Cancer Center
   PI: Dr. Apostolia Tsimberidou, Department of Investigational Therapies

Next Milestones

1. Treatment of first patients with multiple T-cell products to defined targets

2. By end 2018: demonstration of safety and efficacy
1. First target and T-cell receptor (TCR) successfully identified and characterized
2. Retroviral construct expressing the TCR for gene therapy successfully manufactured
3. GMP T-cell manufacturing established
4. Clinical Study approved by FDA within 30d
5. Trial started in September 2017 at MD Anderson Cancer Center
   PI: Dr. George Blumenschein, Department of Thoracic Cancer
6. Second target and TCR successfully identified for second ACTengine program

Achievements

Next Milestones

1. By end 2017: Treatment of first patient with gene-engineered approach
2. By end 2018: demonstration of safety and efficacy
3. FDA pre-IND meeting scheduled for second ACTengine program
Research & Development Progress

• Successfully completed pre-clinical development of ACT programs on time
• Presented pre-clinical data packages for first two program to FDA and received principle green light to proceed to first-in-man studies
• Achieved IND approval by FDA for ACTolog Personalized Immunotherapy Program → Clinical trial started at MD Anderson Cancer Center in July 2017
• Achieved IND approval by FDA for ACTengine Gene-engineered Program → clinical trial started at MD Anderson Cancer Center in September 2017
• Preparing IND submission for third IND

Business Progress

• Awarded up to $19.7m of CPRIT funding, matched with $40m of committed private equity funding
• Signed broad collaboration with MD Anderson Cancer Center
• Further validation of Immatics’ Immuno-Oncology target platform through collaboration with Amgen in 2017 ($30m upfront, >$1b milestones)
• Immatics closed $58m private equity funding in 2017
Commitment to building a sustainable company in Houston, Texas

- Moved into 15,000 sq ft Life Science Plaza laboratory & office facility
- Hired 45 people, all based in Houston
- Two senior management members moved from Germany to Houston (TX)

Steffen Walter (with son)
Chief Scientific Officer Immatics US
Moved to Houston (TX) in 2015

Harpreet Singh (with Longhorn)
Chief Executive Officer Immatics US
Moved to Houston (TX) in 2016
Thank you

Immatics US, Inc.

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