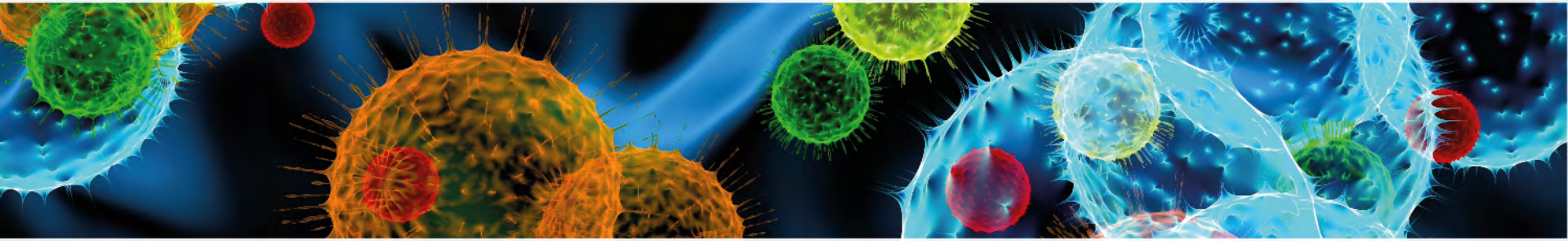
# NOVEL TARGETED CANCER IMMUNOTHERAPIES MADE IN TEXAS

CPRIT's Product Development Research Showcase
November 13, 2017

Harpreet Singh, PhD, President & CEO, Immatics US Inc.



**Immatics US Inc.**

# Immatics – A World Leader in Cancer Immunotherapy

- **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<br>(90 FTEs Germany) |



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# Cancer Immunotherapy: A New Era


Issue of 20 December 2013

## 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**



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# Cancer Immunotherapy: A New Era


Issue of 20 December 2013

**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



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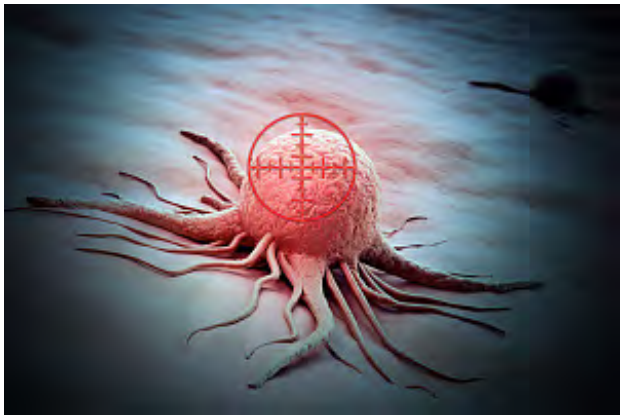
# The Problem: The Missing Targets



| | MODE OF ACTION | TARGET SPACE | APPLICATION |
|---|---|---|---|
| CHECKPOINT INHIBITORS | Non-targeted | - | Cancer with high mutation rate |
| CAR-T CELL THERAPY | Targeted | <25% | Mainly liquid cancers |
| TCR T-CELL THERAPY | Targeted | 100% | All cancers including solid cancers |

**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**



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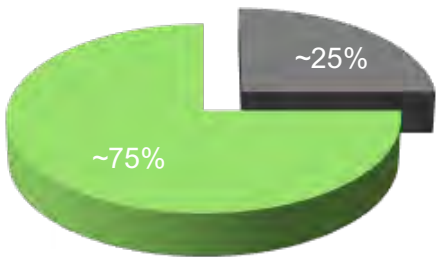
# The solution: accessing the intracellular target space

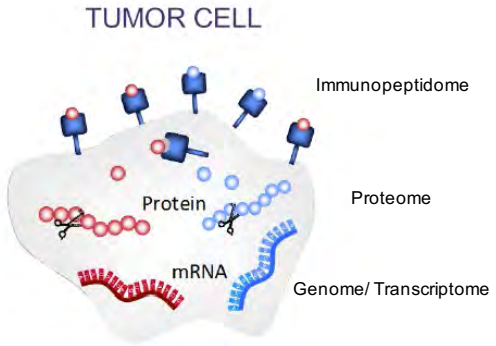
- The number of surface protein targets accessible to mAb and CAR-T approaches is limited
- There are 3-4 times more intracellular targets than surface protein targets
- The T-cell receptor allows access to the intracellular target space via HLA-peptide presentation – the target space discovered and 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[2]**




[2] Uhlen et al., Science 2015

**TCR- vs. CAR/mAb- based approach**




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



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# 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 |

**LC-MS/MS**
**N>600 tumor samples**
RNASeq
N>13000 tumors


**LC-MS/MS**
**N>500 normals**
RNASeq
N>8000 normals

## 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**

| 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 |


Weinschenk et al., Cancer Res (2001)
Walter, Weinschenk et al., Nature Med (2012)
Yadav et al., Nature (2014)

# 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

***CPRIT Established Investigator Award Recipient***

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

## IMMATICS US, INC.

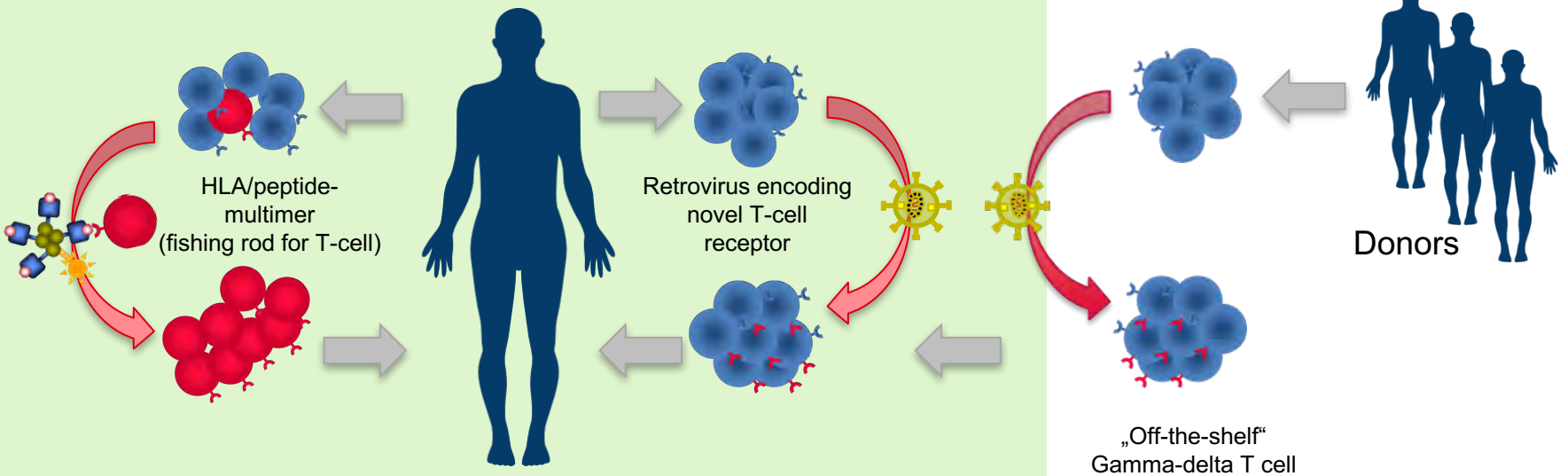
- Co-launched 2015 by Immatics Germany and MD Anderson (holds minority position in Immatics US)
- Location: 15,000 sqft facility at Life Science Plaza, Texas Medical Center Campus, Houston, TX
- Setup of a **state-of-the-art research and development** and **GMP manufacturing** facilities in Houston
-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

# Adoptive Cell Therapy (ACT) Development Tracks

**ACTolog®**
T cells: autologous
TCR: endogenous

**ACTengine®**
T cells: autologous
TCR: engineered

**ACTallo®**
T cells: allogeneic
TCR: engineered




Co-funded by CPRIT



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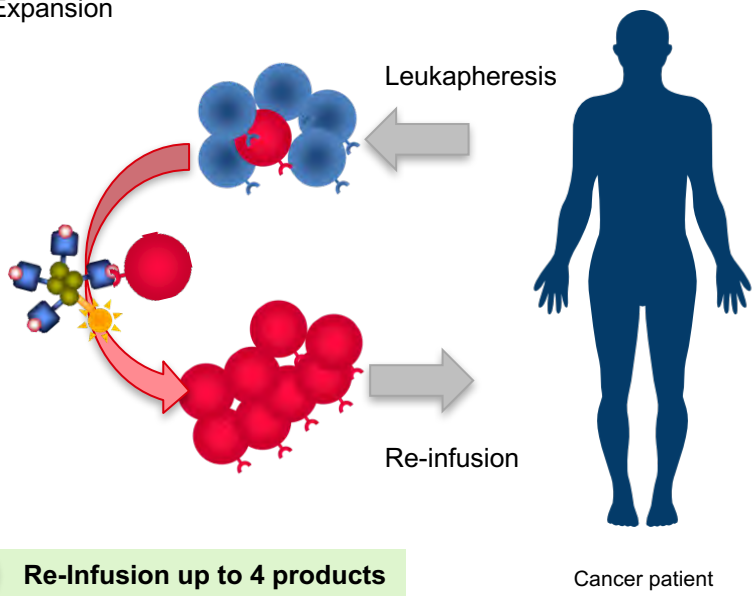
# ACTolog® - Concept & Pioneering Work by Prof. Yee

**1 Tumor target**

- Biomarker profiling
- Pre-defined target warehouse

**2 T-cell generation process**

- Identification of specific cells
- Expansion



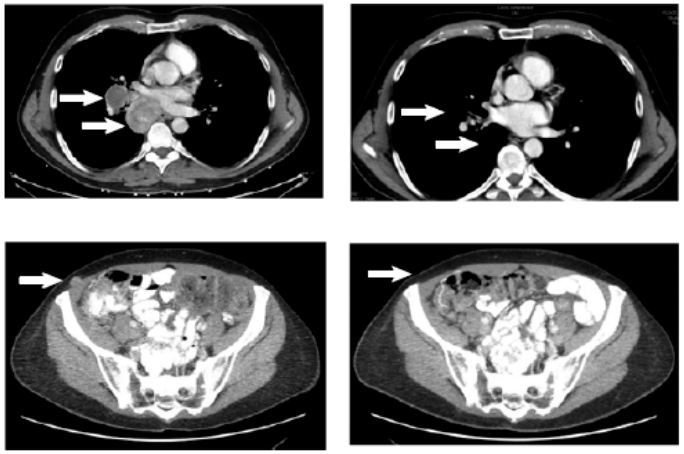

**3 Re-Infusion up to 4 products**

- 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





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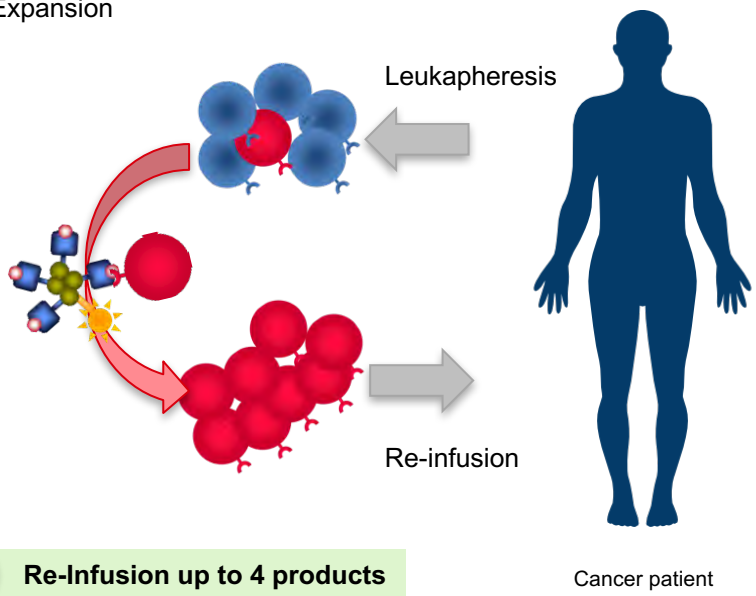
# ACTolog® - Progress update

**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

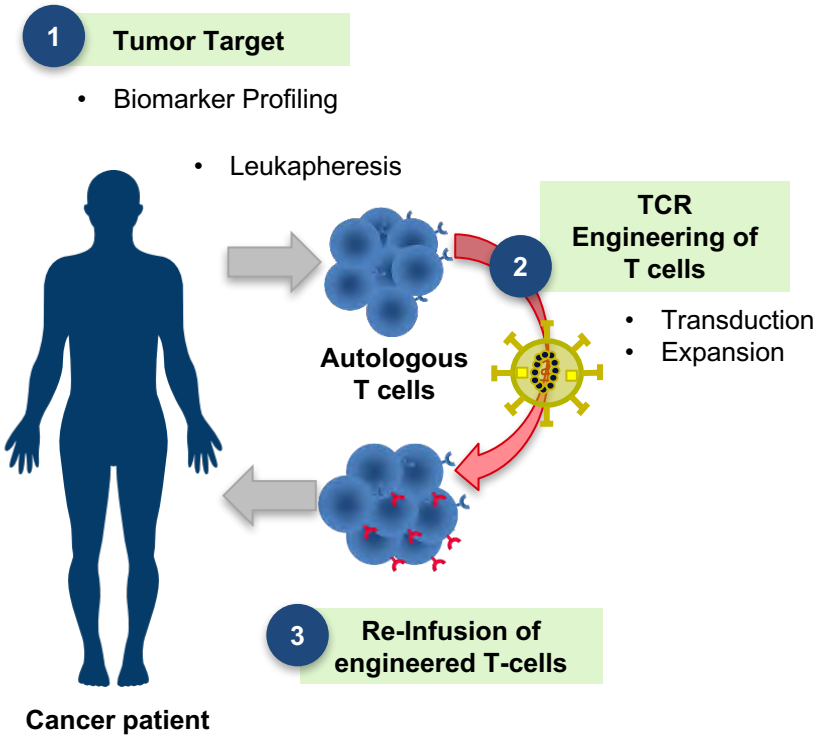
## Achievements

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

# ACTengine® - Concept & Progress update




## Achievements

1. **First target and T-cell receptor (TCR)** successfully identified and characterized
2. Retroviral construct expressing the TCR for **gene therapy** sucessfully 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

## 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

# Immatics US – Summary of Progress in last 24 months

## 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

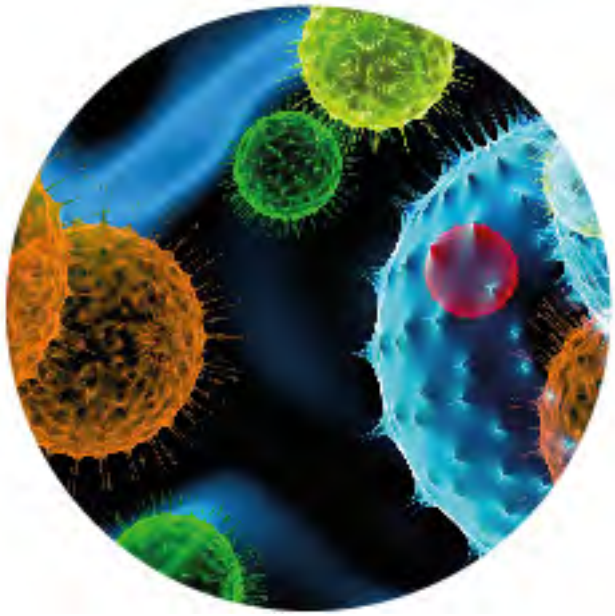
# Immatics US – Summary of Progress in last 24 months

**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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