MedImmune
Delivering the next wave of scientific innovation

Bahija Jallal, Executive Vice President, MedImmune
Building on the fundamentals

Next wave of science
MedImmune has a 25+ year history in biologics; pioneering scientists are still driving discoveries today.

- **RespiGam**
  - Gail Wasserman, PhD
  - Biopharmaceutical Dev.
  - Pennsylvania State Uni.
  - Montclair State Uni.
  - 1996

- **Humira**
  - Mike McCarthy, MD, MPH, MS
  - Infectious Diseases / Vaccines
  - U. Maryland University College
  - Georgetown U. School of Med.
  - 2002

- **Cytogam**
  - Tris Vaughan, PhD
  - Antibody Discovery & Protein Engineering
  - University of Toronto
  - University of Leeds
  - 2003

- **Synagis**
  - Hong Jin, PhD
  - Infectious Diseases / Vaccines
  - Northwestern Uni.
  - Glasgow Uni.
  - 2011

- **Gardasil**
  - JoAnn Suzich, PhD
  - Infectious Disease / Vaccines
  - Purdue University
  - 2006

- **Flumist Quadrivalent**
  - Mark Schenerman, PhD
  - Biopharmaceutical Dev.
  - Cornell University
  - University of Florida
  - 2009

- **Cervarix**
  - Mike McCarthy, MD, MPH, MS
  - Infectious Diseases / Vaccines
  - U. Maryland University College
  - Georgetown U. School of Med.
  - 2009
MedImmune continues to attract world class scientists with strong expertise in areas of interest

Yong-Jun Liu, MD, PhD  
Head of Research  
*Baylor Research Institute Chief Scientific Officer and Director of Immunology Research*

David Howe, MD  
Autoimmunity  
*Cornell University  
University of Toronto  
Edinburgh U. Medical School*

Brett Hall, PhD  
Translational Science - Oncology  
*West Virginia University  
Ohio State University*

Jiping Zha, MD, PhD  
Translational Medicine - Oncology  
*U. Texas Southwestern Med Ctr Dallas  
Harvard Medical School  
University of Tennessee  
Shanghai Medical University*

Jack Ratchford, MD  
Neuro-Immunology  
*Johns Hopkins U. School of Medicine  
Columbia U. College of Physicians and Surgeons*

Jacob Wesley, PharmD, MS  
Oncology  
*Johns Hopkins University  
University of Maryland*

Eliezer Katz, MD  
Neuro-Inflammation  
*U. of Massachusetts Medical Center  
Hebrew U. - Hadassah Medical School*

John Kurland, PhD  
Translational Medicine – Oncology  
*Cold Spring Harbor Laboratory  
U. Texas M. D. Anderson Cancer Center*
MedImmune has a collaborative work environment where staff are encouraged to publish & innovate
Our sustainable pipeline is built on excellence in science

- Strength in immunology
- Expertise in technology & protein engineering
- Excellence in translational research
MedImmune’s strong heritage in immunology is leveraged across therapeutic areas

- **Respiratory, inflammatory, autoimmune diseases**
  - Tempering overactive or inappropriate immunity

- **Oncology: Immuno-oncology therapies**
  - Harnessing / activating the immune system

- **Neurological diseases**
  - Chronic inflammation (unfolded protein response)

- **Cardiovascular & metabolic diseases**
  - Chronic inflammation

- **Infectious diseases / vaccines**
  - Essential for combat of pathogens
Disease biology drives our tech focus: Novel (non mAb) drug formats represent >50% of our research portfolio

Deep “toolkit” of non-mAb approaches…

...and growing as a proportion of the preclinical pipeline
Personalised healthcare is a core principle: More than 80% of our biologics portfolio employs a PHC approach

**Example: PD-L1**

PD-L1 protein expression may not be an absolute determinant of response...we leverage multiple tools to identify responders

- **Genomics and proteomics**
- **Flow cytometry**
- **Tumour cell Target expression**
- **Circulating Tumour cells**
- **Antibody and TCR diversity**
Building on the fundamentals

Next wave of science
MedImmune’s Research & Early Development portfolio is robust with emphasis on core TAs

<table>
<thead>
<tr>
<th>Lead Optimisation</th>
<th>Pre-clinical</th>
<th>Phase I</th>
<th>Phase IIa</th>
<th>Phase IIb</th>
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10 – MedImmune
MedImmune’s programme for Sjögren's employs the novel Tn3 scaffold to avoid mAb-related complications

**Target**
- Blocks co-stimulatory path for CD40L on T cells to bind to CD40 on B cells

**Rationale**
- mAbs efficacious in animal models
- mAbs tested in the clinic with some positive data, but terminated due to blood clots

**Differentiation**
- Tn3 scaffold is a novel non-mAb technology; avoids blood clotting characteristic of anti-CD40L mAbs
- First small protein technology at MEDI to enter clinic

**Platelet Aggregation**

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<tr>
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<th>Biogen 5c8</th>
<th>MEDI4920</th>
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<tr>
<td>400nM</td>
<td>100%</td>
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<tr>
<td>200nM</td>
<td>50%</td>
<td>30%</td>
</tr>
<tr>
<td>100nM</td>
<td>25%</td>
<td>15%</td>
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**MEDI4920:**

- MedImmune
MedImmune’s novel ADC candidate employs the PBD payload and demonstrates early efficacy against cancer

**Target**
- Cancer stem cell target
- Limited expression in normal tissues

**Indication**
- Overexpressed in several tumor types
  - Lung
  - Breast

**Candidate**
- Novel ADC conjugated with PBD payload
- Tumor regression after single dose

**ADC:**
H1975 NSCLC xenograft: Tumor regression with single dose ADC

![Graph showing tumor regression with different treatment conditions](image)

**World ADC Awards**
Sunday October 26th 2014

*Best Scientific Innovation:*
Winner: PBDs (Spirogen)
We are building our early ADC pipeline; vigorously pursuing a broad range of oncology targets

- Forecast is subject to project attrition
- Target discovery activities have launched additional projects for IND delivery beyond 2017
MedImmune is progressing a next generation, extended half-life mAb for RSV

**Target**
- Novel, neutralizing epitope on the RSV F protein, located on the surface of the virion

**Indication**
- Passive immunization of all infants entering their 1st RSV season
- Children with chronic lung or chronic heart disease entering their 1st and 2nd RSV seasons for the prevention of lower respiratory tract illnesses

**Candidate**
- Binds to novel epitope, neutralizing RSV
- Extended half-life based on proprietary, clinically validated YTE technology

*MEDI8897:

**Serum PK in NHP Model**

- [MAb] μg/ml in serum
- Days post infusion

- MAb
- MAb + YTE
MedImmune is pursuing an innovative multi-functional, bi-specific approach for the treatment of *P. aeruginosa*

**Target #1: PcrV – Virulence**
- Prevents toxin injection into host cells
- High affinity mAb to low density target

**Target #2: Psl – Colonisation Persistence**
- Dual mechanism of action: Clearance and blocks cell adherence
- Lower affinity mAb to high density target

**MEDI3902 :**
- anti-PcrV
- anti-Psl
Protein X presents an opportunity to deliver a step change in diabetes therapy

**Target**
- Novel protein with novel mechanism of action

**Indication**
- Type 2 Diabetes
- Goal
  - Dose-dependent reductions in blood sugar
  - Significantly improved islet health
  - Improved insulin sensitivity

**Candidate**
- May regulate pancreatic β-cell function

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### Protein X:

**Glucose (mM)**

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<tr>
<th>Treatment</th>
<th>Days of treatment</th>
<th>Veh</th>
<th>Low</th>
<th>High</th>
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Data are presented as mean ± SEM n=28 (veh), n=22 (Prot-X groups)

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**Vehicle Control**

**3 mg/kg/d Prot-X**
Summary

We have created a vibrant environment, promoting innovation and scientific excellence

We have a robust, balanced, sustainable portfolio

We are moving beyond mAbs, pioneering the next wave of biologics innovation
We push the boundaries of science to deliver life-changing medicines