

# MedImmune R&D Roadshow

**November 7, 2013**  
**Gaithersburg, Maryland**

# Cautionary Statement Regarding Forward-Looking Statements

In order, among other things, to utilise the 'safe harbour' provisions of the US Private Securities Litigation Reform Act 1995, we are providing the following cautionary statement: This presentation contains certain forward-looking statements with respect to the operations, performance and financial condition of the Group. Although we believe our expectations are based on reasonable assumptions, any forward-looking statements, by their very nature, involve risks and uncertainties and may be influenced by factors that could cause actual outcomes and results to be materially different from those predicted. The forward-looking statements reflect knowledge and information available at the date of preparation of this presentation and AstraZeneca undertakes no obligation to update these forward-looking statements. We identify the forward-looking statements by using the words 'anticipates', 'believes', 'expects', 'intends' and similar expressions in such statements. Important factors that could cause actual results to differ materially from those contained in forward-looking statements, certain of which are beyond our control, include, among other things: the loss or expiration of patents, marketing exclusivity or trade marks, or the risk of failure to obtain patent protection; the risk of substantial adverse litigation/government investigation claims and insufficient insurance coverage; exchange rate fluctuations; the risk that R&D will not yield new products that achieve commercial success; the risk that strategic alliances and acquisitions will be unsuccessful; the impact of competition, price controls and price reductions; taxation risks; the risk of substantial product liability claims; the impact of any delay in the manufacturing, distribution and sale of any of our products; the impact of any failure by third parties to supply materials or services; the risk of failure to manage a crisis; the risk of delay to new product launches; the difficulties of obtaining and maintaining regulatory approvals for products; the risk of failure to observe ongoing regulatory oversight; the risk that new products do not perform as we expect; the risk of environmental liabilities; the risks associated with conducting business in emerging markets; the risk of reputational damage; the risk of product counterfeiting; the risk of failure to successfully implement planned cost reduction measures through productivity initiatives and restructuring programmes; the risk that regulatory approval processes for biosimilars could have an adverse effect on future commercial prospects; the impact of failing to attract and retain key personnel and to successfully engage with our employees and the impact of increasing implementation and enforcement of more stringent anti-bribery and anti-corruption legislation. Nothing in this presentation should be construed as a profit forecast.

# Agenda

## Presentations:

Dr. Bahija Jallal, Executive Vice President, AstraZeneca  
Head of MedImmune

Dr. Bing Yao, Head of Respiratory, Inflammation & Autoimmune iMed

Dr. Ed Bradley, Head of MedImmune Oncology iMed

Q&A

Reception

# MedImmune, the global biologics R&D arm of AstraZeneca

**Dr. Bahija Jallal**  
**Executive Vice President, AstraZeneca**  
**Head of MedImmune**

# Today's Discussion

Enterprise Strategy

MedImmune's Roadmap

# Our Strategic Priorities

1

**Achieve  
scientific  
leadership**

2

**Return  
to growth**

3

**Be a great  
place to work**

# Achieve Scientific Leadership

1

**Achieve  
scientific  
leadership**

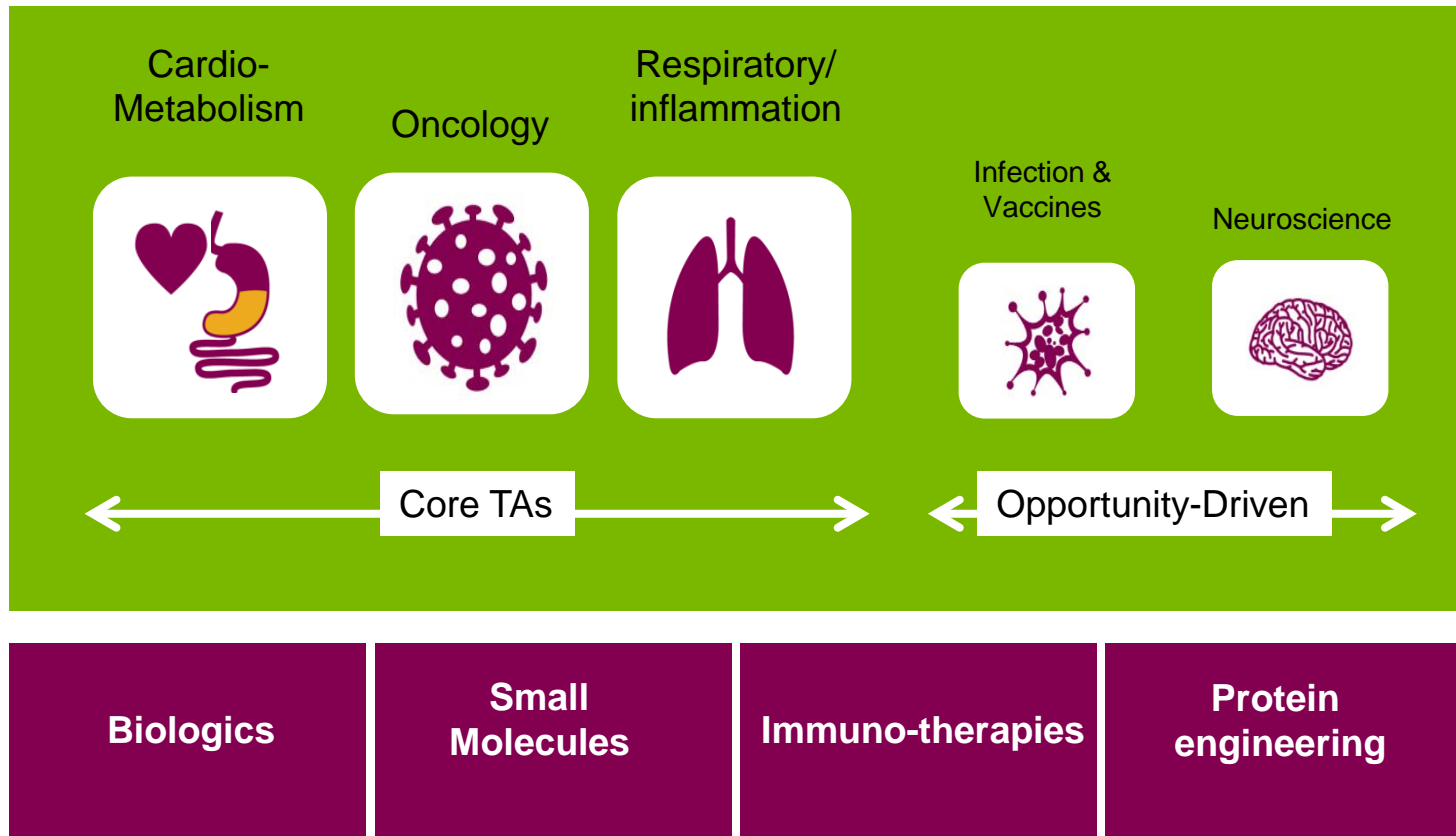
**FOCUS** on distinctive science in 3 core TAs

**PRIORITISE & ACCELERATE** our pipeline

**TRANSFORM** our innovation culture & model

# Our core focus

**FOCUS** on distinctive science  
in 3 core TAs





# Growing late-stage pipeline

PRIORITISE & ACCELERATE  
our pipeline

## Phase 1 - 25 NMEs

### Small molecule

**AZD5363\***  
AKT solid tumours

**AZD2014**  
TORK solid tumours

**volitinib\***  
MET solid tumours

**AZD1208**  
PIM haems

**AZD8186**  
PI3 solid tumours

**AZD9150\***  
STAT3 haems

**AZD9291**  
EGFRm+ solid tumours

**AZD8848\***  
TLR7 asthma

**AZD7594\***  
SGRM COPD

**AZD7624**  
ip38i COPD

**RDEA3170**  
URAT1 gout

**AZD3293\***  
BSECDR Alzheimer's

**ATM AVI**  
BL/BLI SBI

### Biologics

**MEDI0639\***  
DLL-4 solid tumours

**MEDI-565\***  
CEA BiTE GI tumours

**MEDI6469\***  
mOx40 solid tumours

**MEDI4736\***  
PD-L1 solid tumours

**MEDI3617\***  
ANG-2 solid tumours

**MEDI9929\***  
TSLP asthma

**MEDI5872\***  
B7RP1 SLE

**MEDI-551\***  
CD19 MS

**MEDI6012**  
LCAT, ACS

**MEDI4893**  
staph alpha toxin SSI

**MEDI-559**  
PRVV

**MEDI-550**  
Panflu library

## Phase 2 - 23 NMEs

### Small molecule

**selumetinib\***  
MEK solid tumours

**AZD4547**  
FGFR solid tumours

**olaparib**  
PARP-BRCA solid tumours

**AZD5423\***  
iSGRM COPD

**AZD5069**  
CXCR2 asthma

**AZD2115\***  
MABA COPD

**AZD1722\***  
NHE3 ESRD/CKD

**AZD6765**  
NMDA MDD

**AZD5213**  
H3R neuropathic pain

**AZD3241**  
MPO Parkinson's Disease

**AZD5847**  
oxazolidinone TB

**CXL\***  
BLI/cephalosporin MRSA

### Biologics

**MEDI-551\***  
CD19 CLL, DLBCL

**tremelimumab**  
CTLA-4 solid tumours

**MEDI-573\***  
IGF MBC

**benralizumab\***  
IL-5R asthma / COPD

**mavrilimumab\***  
GM-CSFR RA

**MEDI8968\***  
IL-1R COPD, HS

**sifalimumab\***  
IFNa SLE

**MEDI-546\***  
IFNaR SLE

**tralokinumab**  
IL-13 asthma, IPF, UC

**MEDI7183\***  
α4β7 UC, Crohn's

**MEDI2070\***  
IL-23 Crohn's

\* Partnered Product

## Phase 3 / Reg - 8 NMEs

### Small molecule

**lesinurad**  
URAT1 gout

**PT003**  
LABA/LAMA COPD

**Epanova\***  
hypertriglyceridaemia

**naloxegol\***  
opioid induced constipation

**CAZ AVI\***  
BLI/cephalosporin SBI

### Biologics

**moxetumomab\***  
CD22, HCL

**brodalumab\***  
IL-17R psoriasis

**metreleptin\***  
lipodystrophy

## Major Mkt Reg - 5 NMEs

### Small molecule

**Caprelsa**  
EGFR inhibitor MTC

**Brilinta**  
ADP receptor antagonist

**Forxiga\***  
SGLT2 inhibitor

**Zinforo\***  
skin infections

### Biologics

**Q-LAIV Flu**  
Intranasal influenza virus

MedImmune comprises ~50% of the AZ pipeline

Oncology

RIA

CVMD

Neuroscience

Infection

Progressed

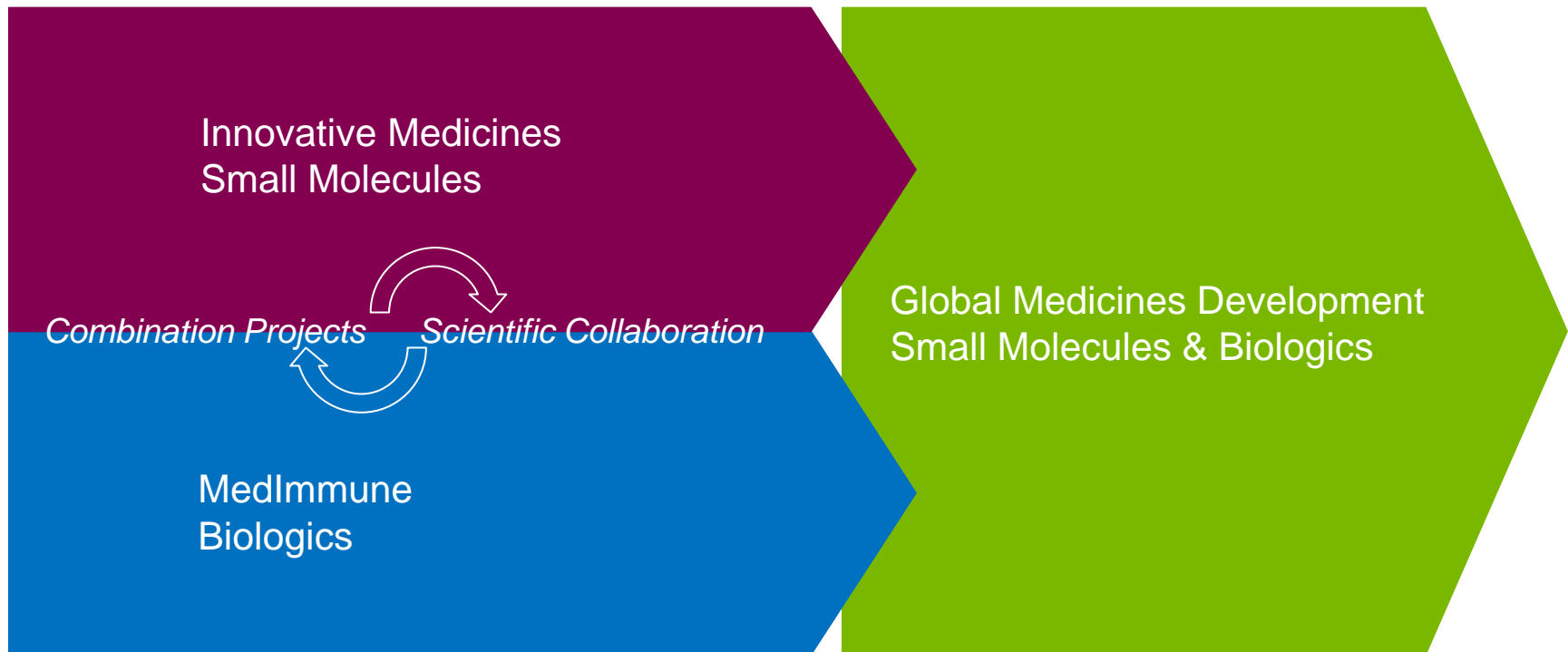
New BD

# Bringing It Together

**TRANSFORM** our innovation culture & model

*“Biotech Organizations”  
Research To POC*

*“Large Pharma”  
Late Stage Development*



# Co-locate around three strategic sites

**TRANSFORM** our innovation culture & model

## Gaithersburg

*Co-locate around biologics/specialty care*



*Proximity to NIH, Johns Hopkins, FDA*

## Cambridge

*Co-locate R&D in world-class science cluster*



*New site in Cambridge with close proximity to University of Cambridge and world class UK bioscience community*

## Mölnadal

*Leverage historical strength Respiratory and CV/Met*



*Connections to Karolinska Institute & Medicon Valley*

# Today's Discussion

**Enterprise Strategy**

**MedImmune's Roadmap**

# Building on a deep heritage of innovation

During the past 25 years, MedImmune has played a role in the following...

RSV

RespiGam

1996

Inflammatory Diseases

**HUMIRA**<sup>®</sup>  
adalimumab

2002

HPV Vaccine

Cervarix<sup>®</sup> 

2009

CMV

 **CYTOGAM**<sup>®</sup>  
Cytomegalovirus Immune Globulin  
Intravenous (Human) (CMV-IVIG)

1998

Flu Vaccine

 **FLUMIST**<sup>®</sup>  
Influenza Vaccine Live,  
Intranasal

2003

SLE

**Benlysta**<sup>®</sup>  
(belimumab) 

2011

RSV

**SYNAGIS**<sup>®</sup>  
PALIVIZUMAB 

1998

HPV Vaccine

 **GARDASIL**<sup>®</sup>

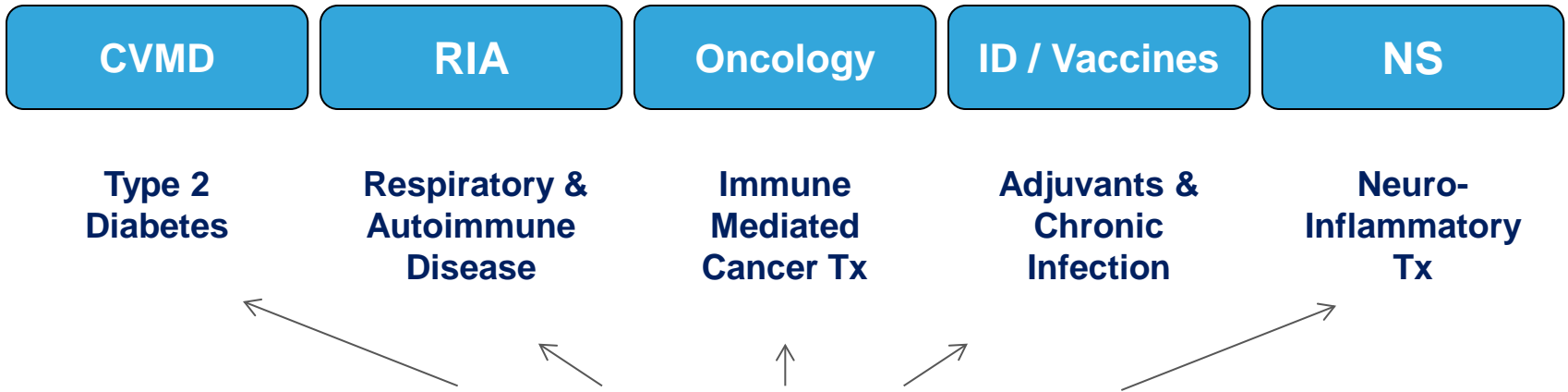
2006

Flu Vaccine

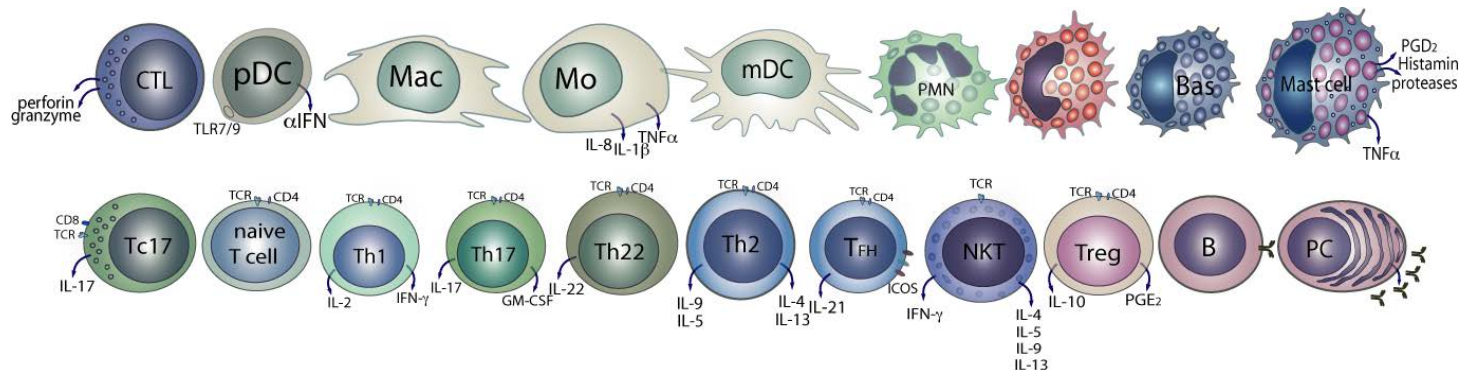
 **FluMist**<sup>®</sup> Quadrivalent  
Influenza Vaccine Live, Intranasal

2012

# Distinctive MedImmune strength in immunology is a foundation across TAs

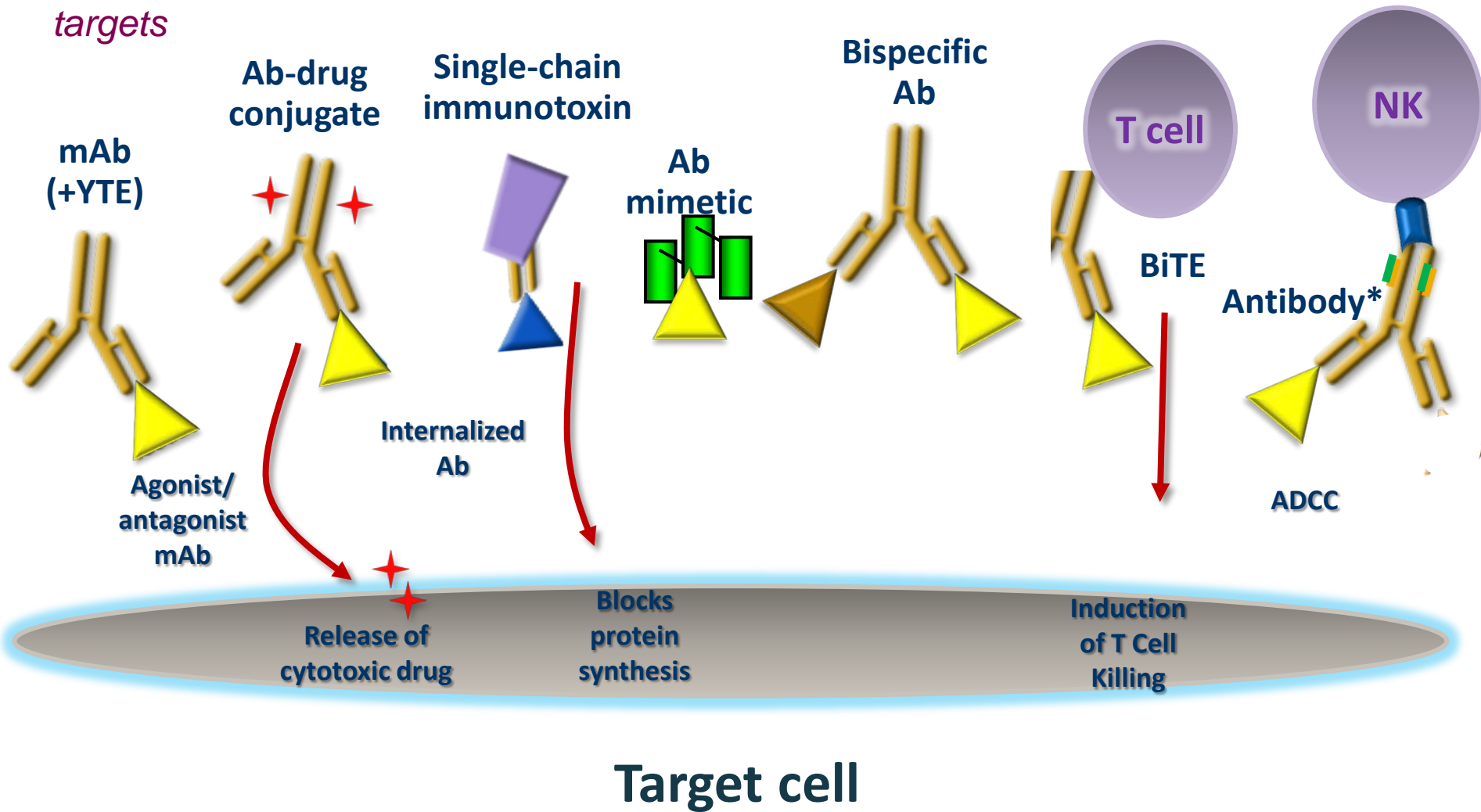


## Deep understanding of immunology biology



# MedImmune Antibody Technologies

*Competitive antibody design and protein engineering toolkit lets us tackle multiple targets*



# Personalized healthcare and diagnostics

**80% of our pipeline has a personalized healthcare approach**

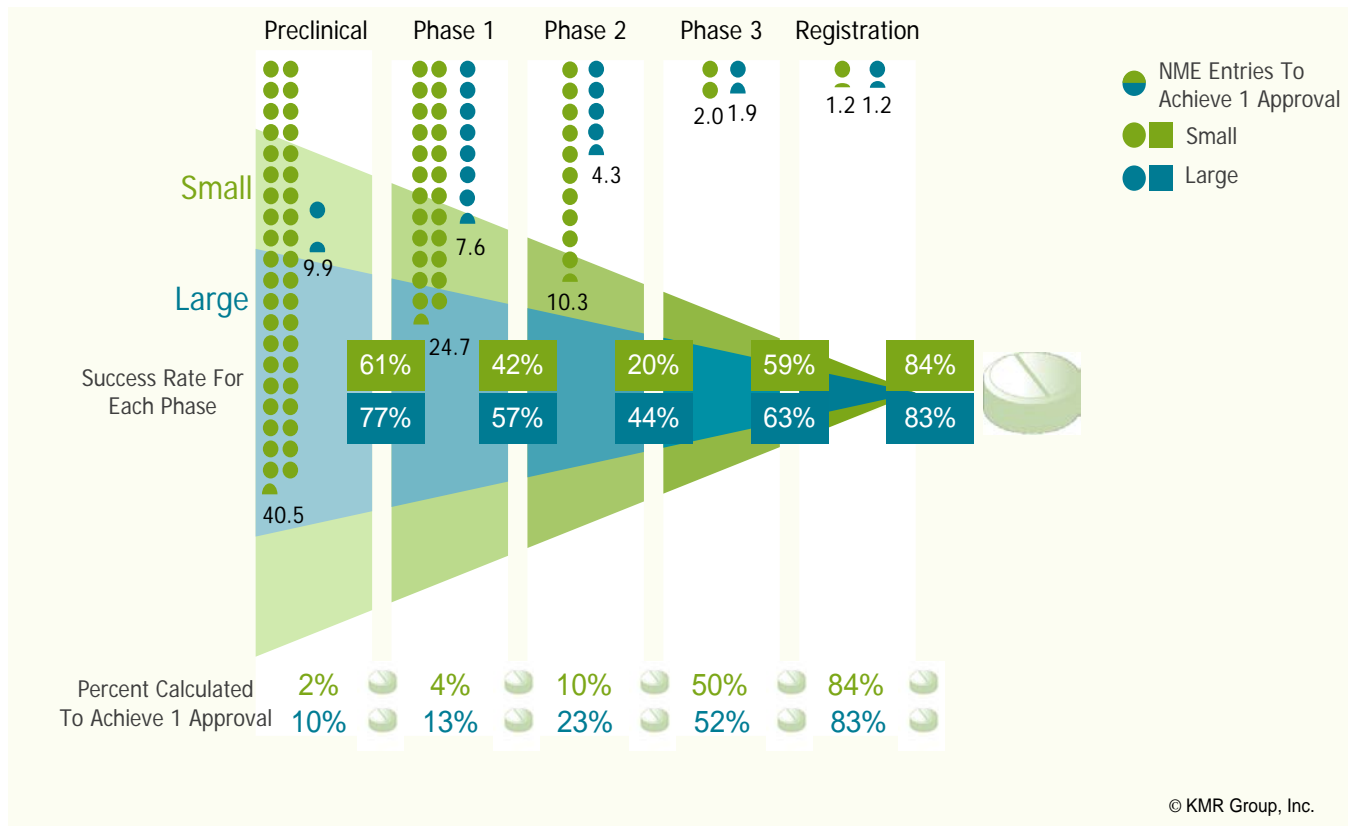
## Meaningful questions being asked by our Personalized Healthcare colleagues:

- What is the right indication to pursue in the clinic?
- What are the patient populations most likely to respond?
- What is the PD biomarker needed to follow target engagement?
- What are the biomarkers for proof of mechanism?
- What are biomarkers of efficacy?
- Do we need a companion diagnostic?

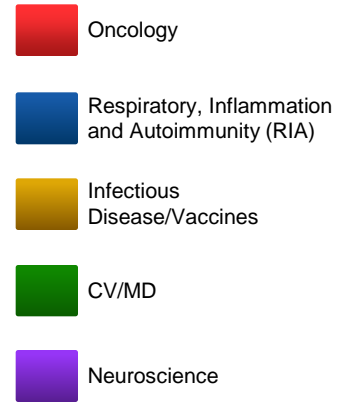


# Characteristics of biologics seem to lead to greater likelihood of success

## NME Success By Molecule Size 2007–2011 Industry Portrait



# Biologics Pipeline

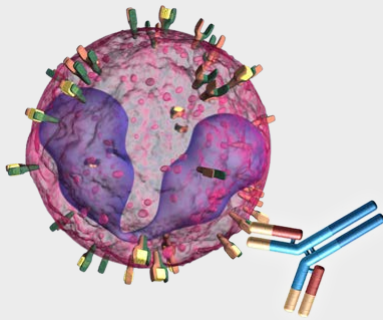


As of August 1, 2013

MedImmune comprises ~50% of the AZ pipeline

# Programs in Phase 3 in 2013

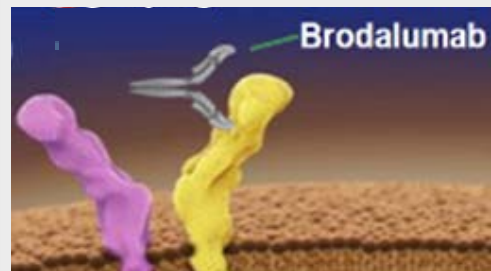
## Benralizumab IL-5R



### Asthma

- Phase 3 started in October

## Brodalumab IL-17RA



### Psoriasis (PsO)

- Phase 3 started Aug 2012
- Estimated biologics license application filing 2015

## Moxetumomab CD22



### Hairy Cell Leukemia (HCL)

- Phase 3 started in May
- Estimated biologics license application filing 2017

# MedImmune's Roadmap

2013-2014

## Immediate priorities

- Deliver mid-stage cohort of assets to Ph3
- Focus on immune-mediated therapies for cancer (IMT-C)
- Continue collaboration/business development (eg Spirogen, Amgen, WuXi AppTec, Amplimmune)

2015-2016

## Mid-term goals

- Deliver next biologics license application
- Capture potential of regional science networks in Maryland, Cambridge and CA

2016+

## Long-term aspiration

- Steady state delivery of important medicines to patients
- Sustainable research engine

# Helping Patients with Respiratory, Inflammation & Autoimmune Diseases

**Dr. Bing Yao, Senior Vice President  
and Head of RIA iMed, MedImmune**



# Vision is to be industry leader in innovative inhaled and targeted therapies for people with asthma, COPD, and IPF

## Unique inhaled therapies

- Symbicort®  
(budesonide/formoterol fumarate dihydrate) Inhalation Aerosol
- Develop novel combinations
- Develop new devices and innovative product

## Innovation-driven targeted therapies

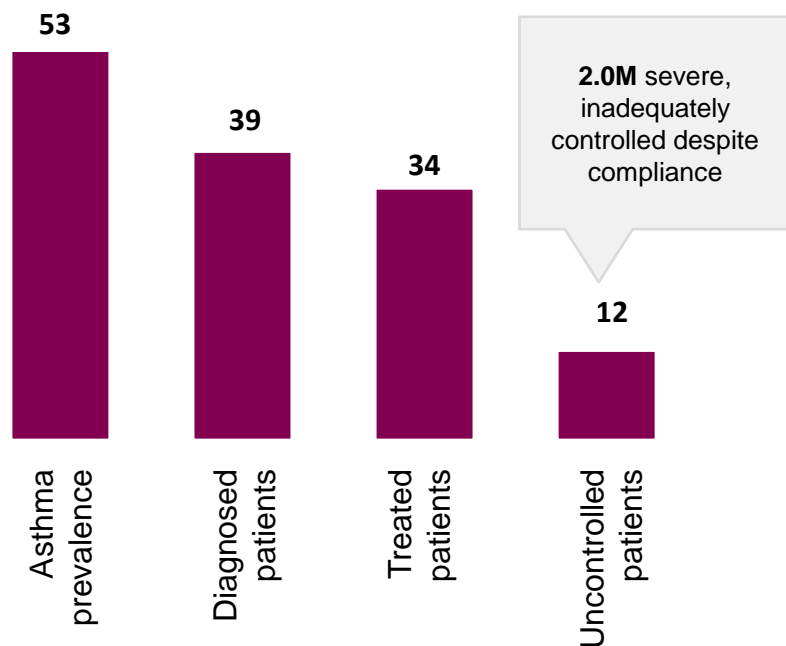
- Understand patient phenotypes (clinical and molecular)
- Develop targeted therapies for complementary patient segments
- Evolve disease management from failure based approach to Dx driven PHC

# Significant unmet needs and opportunity for growth in both asthma and COPD

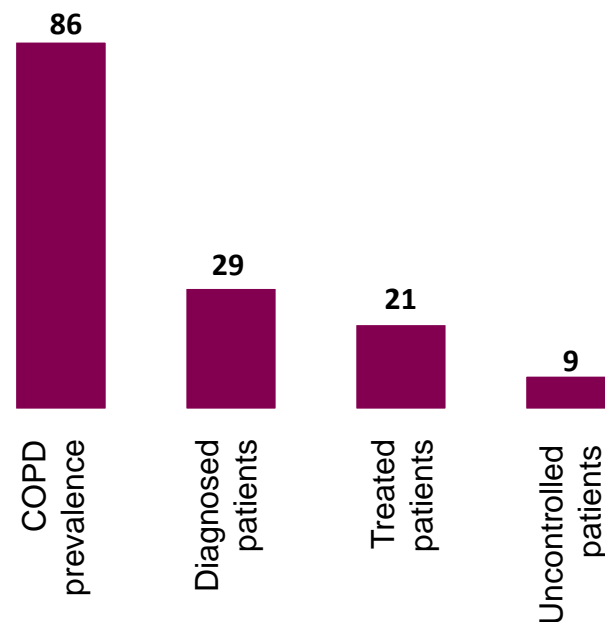
Asthma<sup>1</sup> - \$19 billion, growing 6.5%

COPD<sup>1</sup> - \$15 billion, growing 8.8%

Number of active patients (G7 markets, M)<sup>1</sup>



Number of active patients (G7 markets, M)<sup>2</sup>



# Unmet need and shared biology presents a significant opportunity in autoimmune diseases

Explore shared biology and pathway

## Cytokines

e.g., IFN $\alpha$ , IL17, IL23

## T-Cell Co-stimulators

e.g., B7RP

## Effector Macrophages

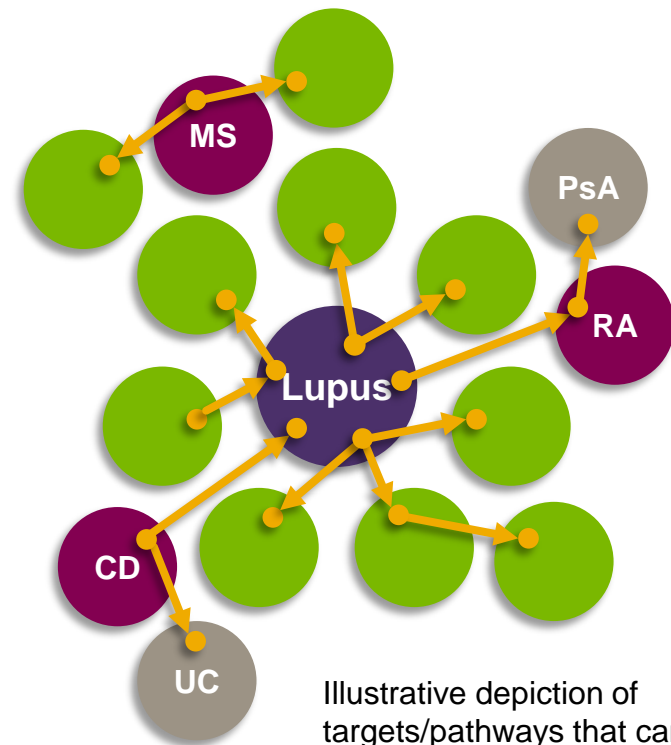
e.g., GM-CSF

## T Regulatory cells

## B-cell Autoantibodies

e.g., CD-19

Pursue potential therapeutic spanning multiple indications



Illustrative depiction of targets/pathways that can be common across diseases

Lupus

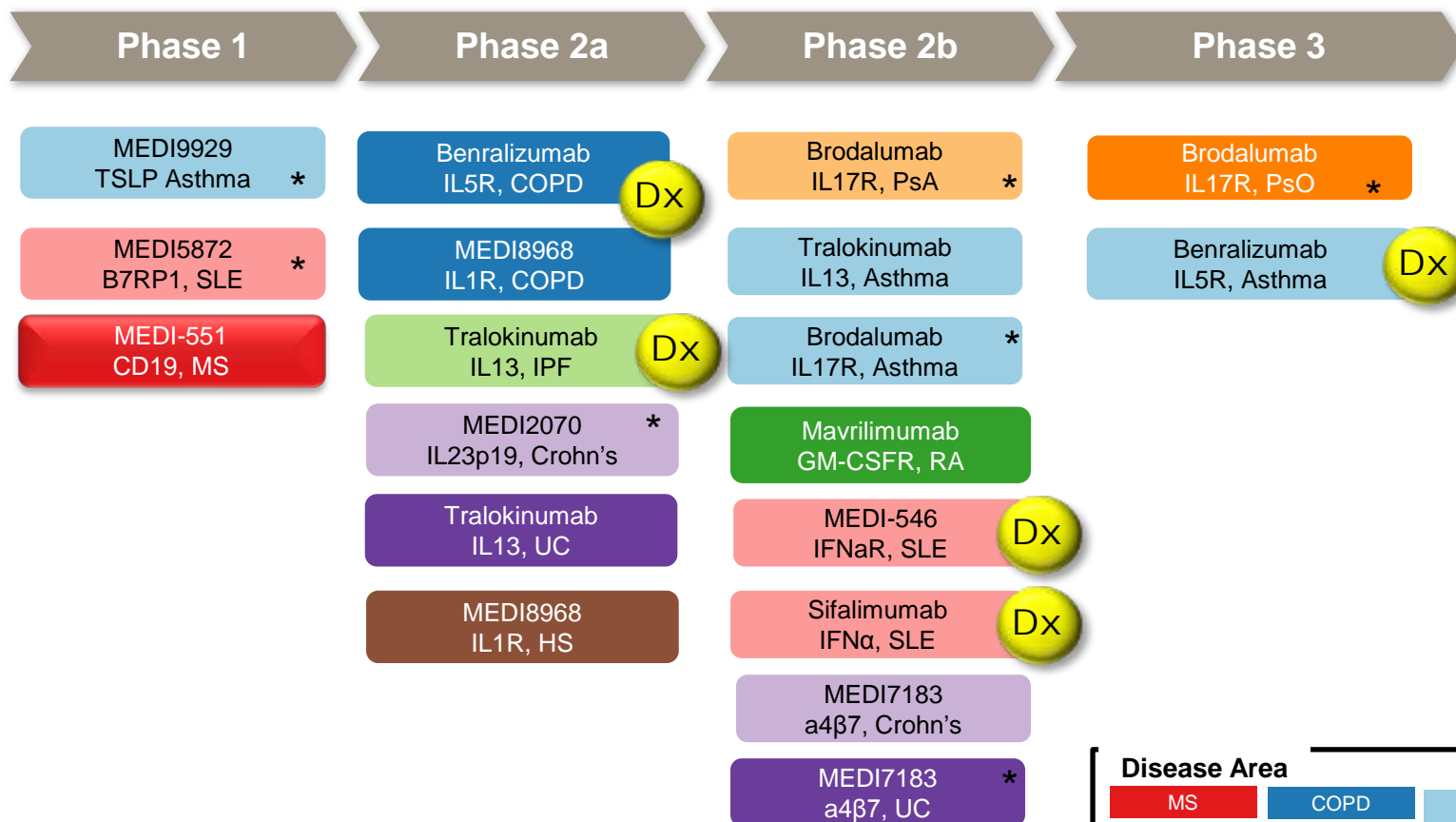
Opportunistic

New indications'

LCM



# A robust respiratory and autoimmune disease portfolio



with diagnostic

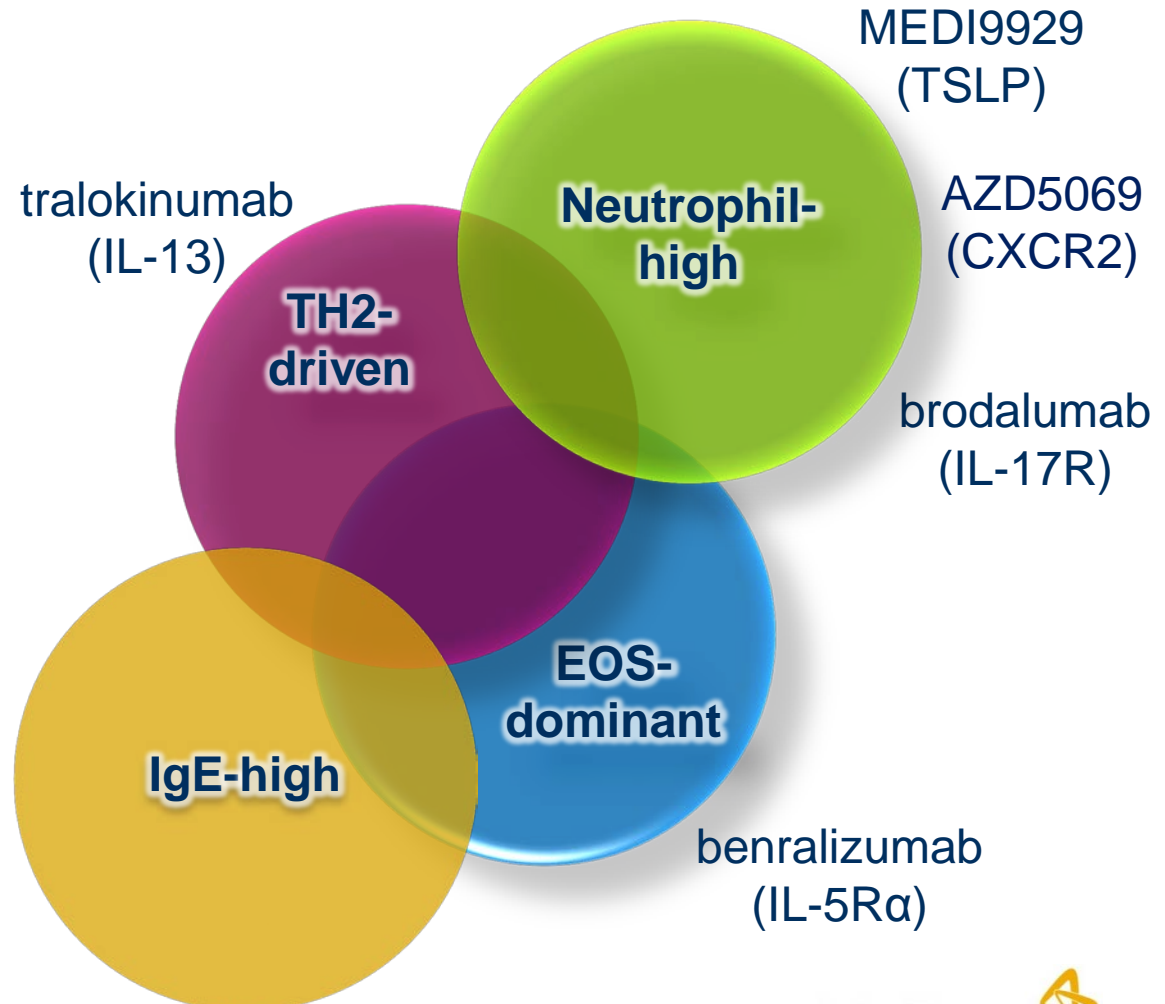
\* Amgen collaboration

Disease Area		
MS	COPD	Asthma
PsA	IPF	UC
PsO	RA	Gout
Crohn's	SLE	HS

# Personalized healthcare approach: *targeting different segments of the severe asthma*

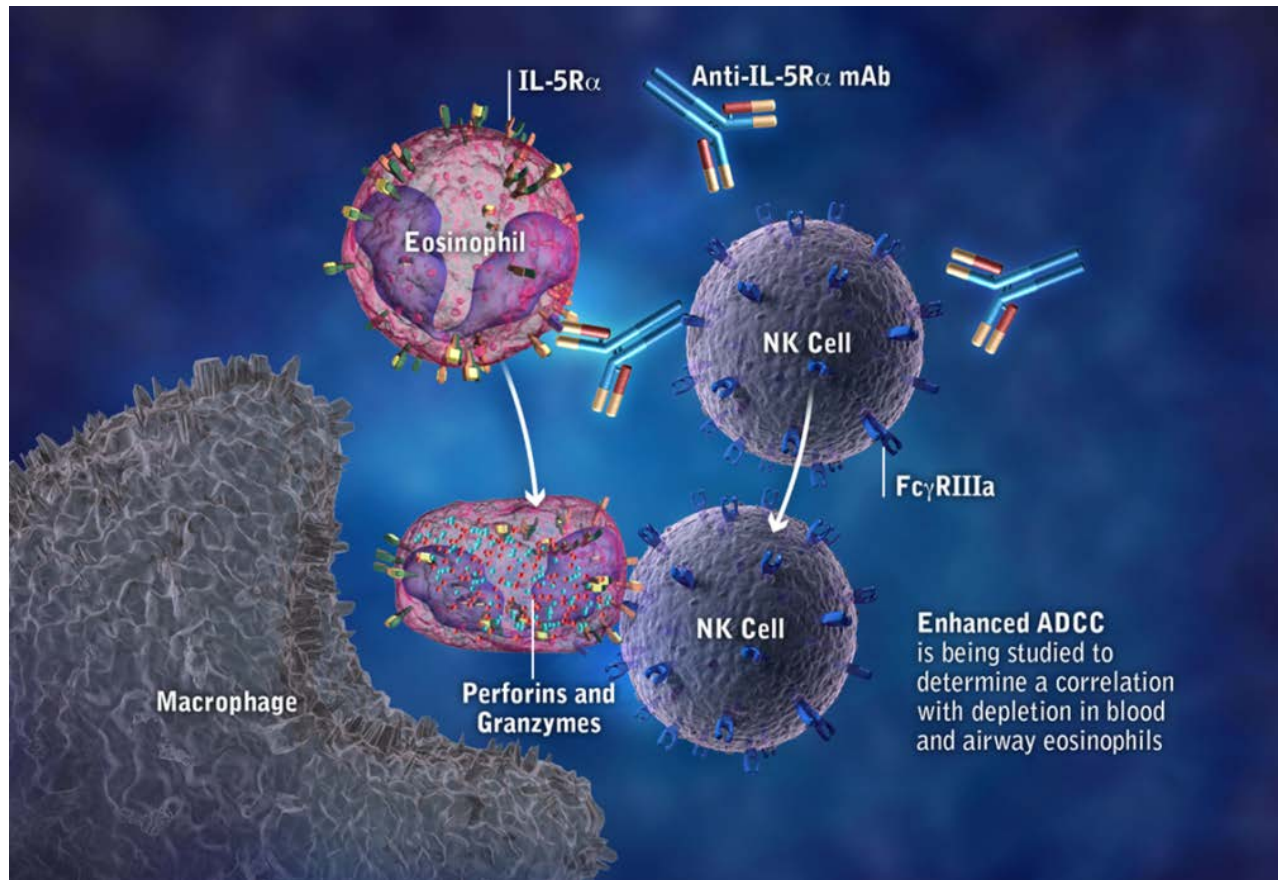
Asthma is a highly heterogeneous disease

- Developing understanding of underlying cause
- Studying patient subtypes
- Developing diagnostics
- Tailoring therapies



# 1) Benralizumab (MEDI-563): asthma (Ph3) *targeted therapy for severe eosinophilic asthma*

## Mechanism of Action: anti-IL-5R $\alpha$

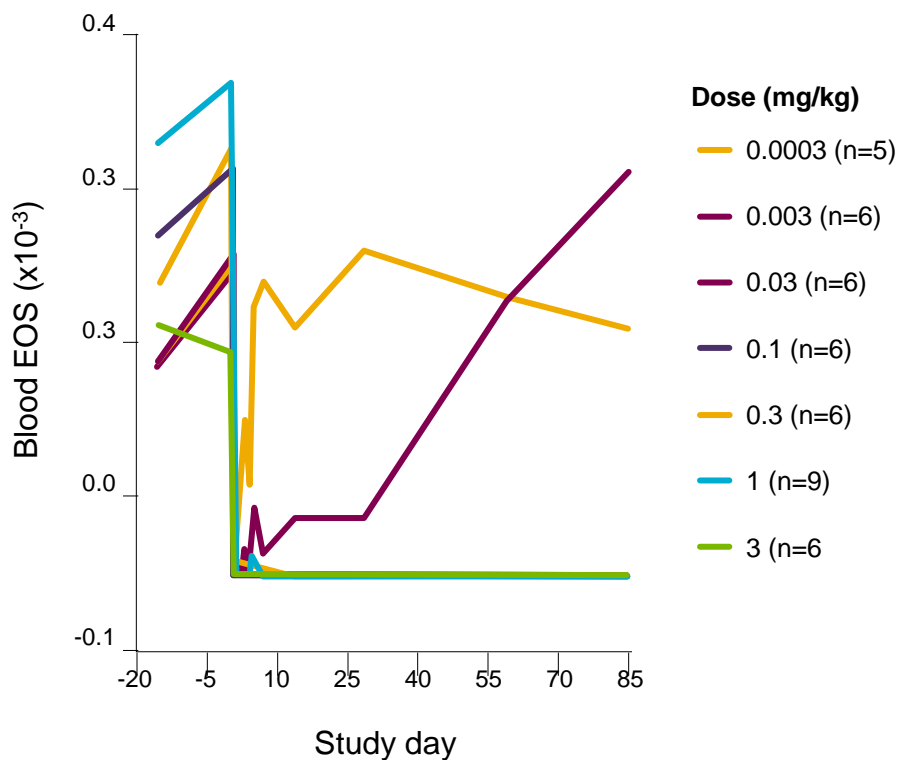


## Eosinophilic asthma

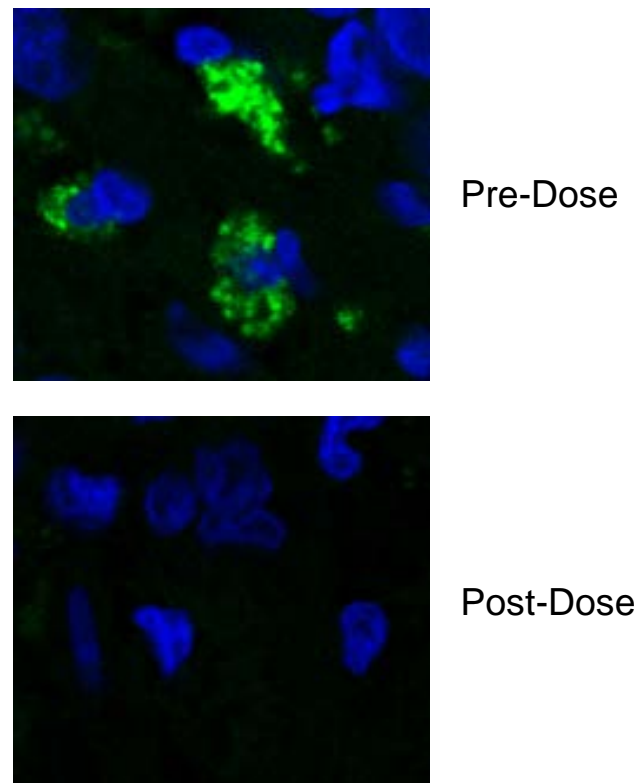
- Asthmatics with eosinophilia represent ~40-60% of severe asthmatics
- Eosinophil count associated with exacerbation
- Binding with high affinity to IL-5R $\alpha$  depletes eosinophils

# Benralizumab potently depletes eosinophils

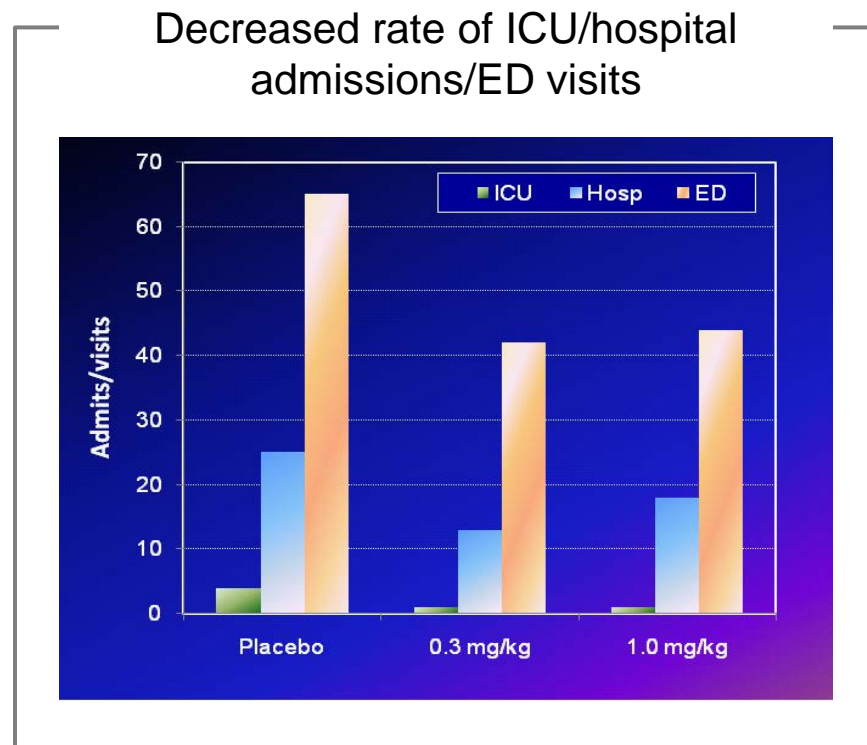
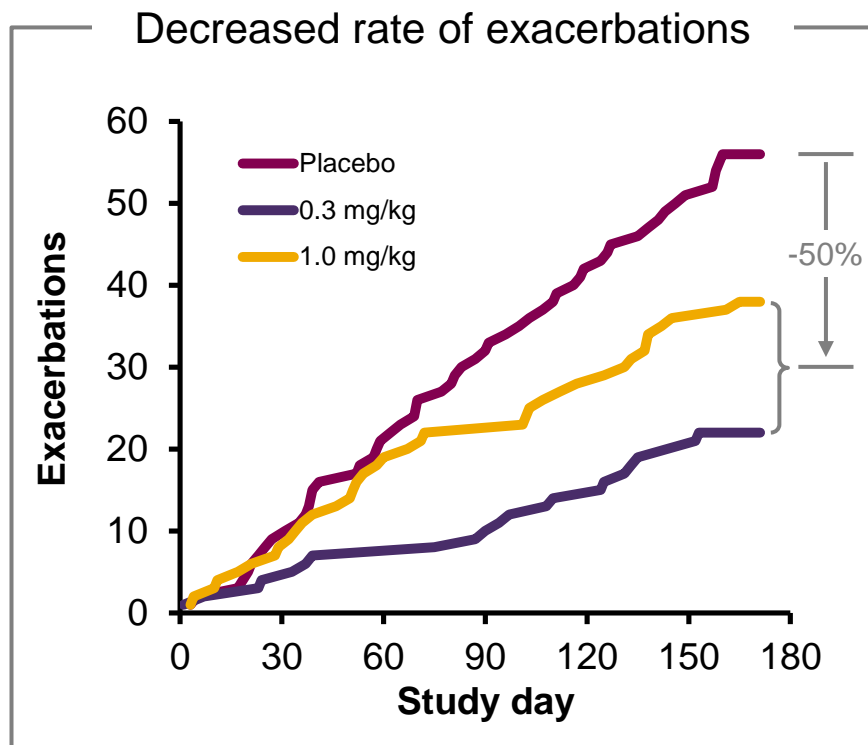
## Eosinophil depletion in periphery



## Eosinophil depletion in lung



# Phase 2a showed reduced exacerbations and hospitalizations in a high risk patient population



# Benralizumab with novel mechanism of action enters Ph3 for eosinophilic patients

## Differentiation

- Receptor vs. ligand approach
- Q4/8W subcutaneous dosing
- Complete eosinophil depletion with potential for improved clinical outcome<sup>1</sup>
- Patient selection approach through blood test; targeted to discriminate eosinophilia

## Development plan

### Phase 3 start asthma

- Announced the Phase III Windward program on 30 October

### Phase 2b asthma

- Patients with elevated eosinophils had a statistically significant reduction in exacerbation rate and improvements in lung function and asthma symptoms
- Efficacy and safety data supported progression to Ph3
- Results expected to be shared in 1H 2014

### Phase 2a COPD

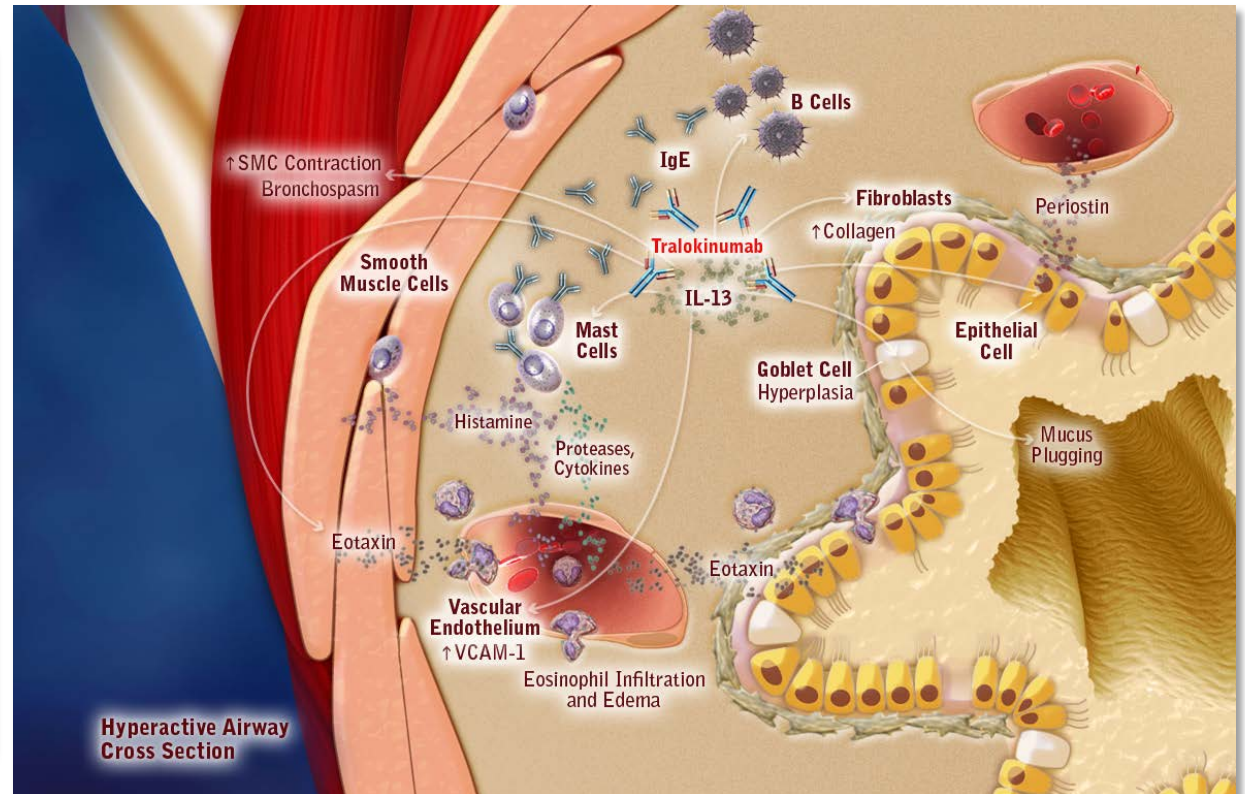
- Severe COPD with elevated eosinophils
- Study completed and decision pending

<sup>1</sup> Depletion was reversible and was observed up to 3 months. Not seen in all doses

## 2) Tralokinumab (CAT-354): asthma Ph2b *targeted against a cytokine central to asthma*

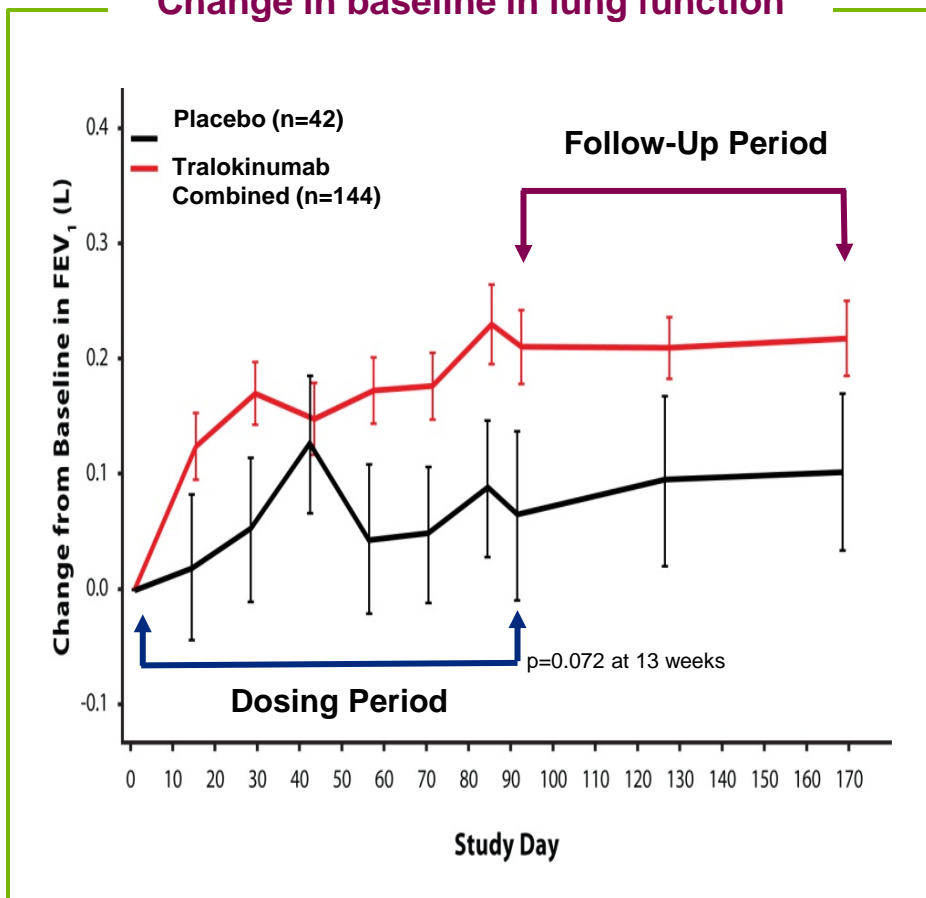
### Mechanism of Action: Anti-IL-13

- Target severe, inadequately controlled asthma
- Tralokinumab a fully human antibody targeting IL-13
- Key cytokine involved in many aspects of asthma
- Validated target from pre-clinical and clinical studies



# Tralokinumab has demonstrated clinical response

## Change in baseline in lung function



## Development plan

### Phase IIB asthma

- Assesses exacerbation reduction vs. placebo in severe uncontrolled asthma
- Evaluating spectrum of blood and serum biomarkers
- Decision on whether to move to Ph3 expected in H1'14

### Other

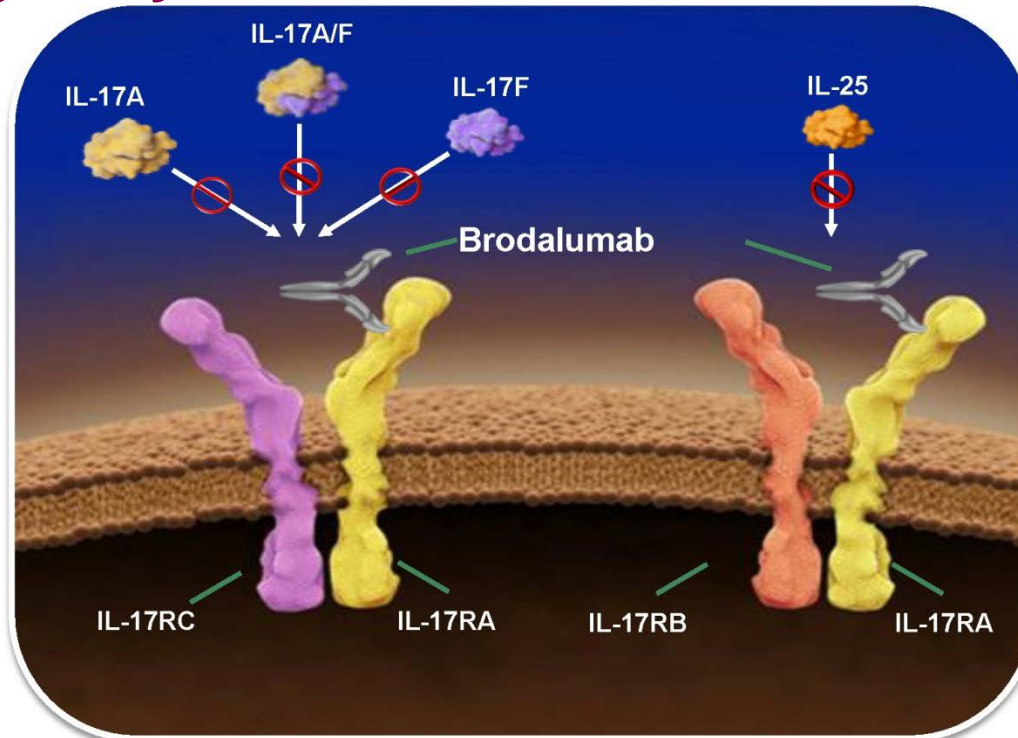
- IPF as respiratory Life Cycle opportunity

Piper E et al. Eur Respir J. 2013, 41:330-8

FEV<sub>1</sub> = Forced Expiratory Volume  
IPF = Idiopathic Pulmonary Fibrosis



### 3) Brodalumab: high unmet needs remain for psoriasis and IL-17 family of cytokines are drivers of the diseases



- ~12M diagnosed PsO patients in the 7 major markets\*
- Plaques that can cover >10% of the body
- Severe disease significantly impacts quality of life due to location of plaques, pain, bleeding, and arthritis
- Need new treatment options for rapid clearance of plaque and improve quality of life

Brodalumab is being co-developed by Amgen and AstraZeneca/MedImmune.

# Brodalumab (Ph3) Ph1/2 Results



Percentage Improvement in PASI Scores over Time.

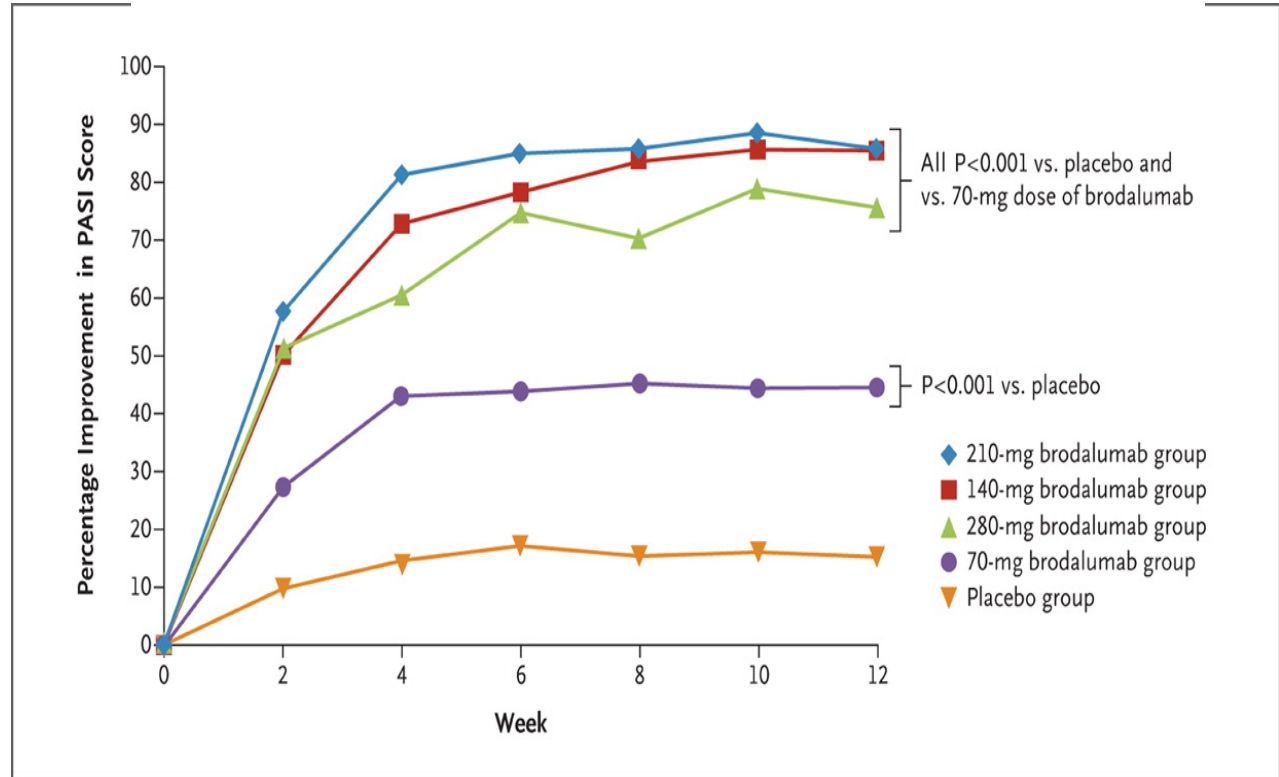


Figure 1. Percentage Improvement in PASI Scores over Time. The P value for the comparison of the 70-mg dose of brodalumab with placebo ( $P < 0.001$ ) is for all the time points except week 2, for which the P value was 0.002. PASI denotes psoriasis area-and-severity index.

Papp KA et al. N Engl J Med 2012;366:1181-1189.

Dosing	Place bo	140 mg q2wk	210 mg q2wk
PASI 90, n(%)	0.0	71.8	75.0
PASI 100, n(%)	0.0	38.5	62.5

# Brodalumab: Psoriatic Arthritis Phase 2 Study Summary

- Phase 2 study of brodalumab demonstrated efficacy in PsA with acceptable safety profile
- Primary endpoint of study was met with both doses of brodalumab (140 mg Q2W and 280 mg QW) demonstrating superiority to placebo for ACR 20 responses
- No new safety findings observed for brodalumab
- Brodalumab will be further evaluated in Phase 3 PsA studies

# Additional Phase I and II Investigational Programs

Disease area	Asset	Mechanism	Phase
<b>COPD</b>	benralizumab	IL-5R $\alpha$	II
	MEDI8968	IL1-R	II
<b>Asthma</b>	tralokinumab	IL-13	II
	brodalumab	anti-IL-17R	II
	MEDI9929	TSLP	I
<b>IPF</b>	tralokinumab	IL-13	II
<b>Psoriatic Arthritis</b>	brodalumab	anti-IL-17R	II

Disease area	Asset	Mechanism	Phase
<b>Crohn's Disease</b>	MEDI2070	IL-23	II
	MEDI7183	$\alpha$ 4 $\beta$ 7	II
<b>SLE</b>	MEDI5872	B7RP1	I
	sifalimumab	IFN $\alpha$	II
	MEDI-546	IFN $\alpha$ R	II
<b>MS</b>	MEDI-551	CD19	I
<b>Ulcerative Colitis</b>	tralokinumab	IL-13	II
	MEDI7183	$\alpha$ 4 $\beta$ 7	II
<b>RA</b>	mavrilimumab	GM-CSF	II
<b>HS</b>	MEDI8968	IL1R	II

RDEA3170 and MEDI-551 MS are not shown in the earlier pipeline view which is an NME-only view

# MedImmune's Competitive Advantage in RIA

**Robust pipeline**

**Broad spectrum of respiratory and autoimmune diseases**

**Transformative therapies**

**To evolve treatment paradigm from “failure-based approach” to personalized**

**Accelerated delivery**

**Multiple programs with potential to move into Phase III by the end of 2014**

# Exploring New Approaches in Oncology

**Dr. Ed Bradley, Senior Vice President and  
Head of the Oncology iMed, MedImmune**



# MedImmune Oncology Biologics Strategy

## Specific Immune Targeting

Immune Mediated  
Therapy (IMT)



**Generating potent immunologic response via T cell modulation and other immune cell mechanisms**  
**Potential activity in the majority of tumor cancers**

## Specific Tumor Targeting

Armed antibodies

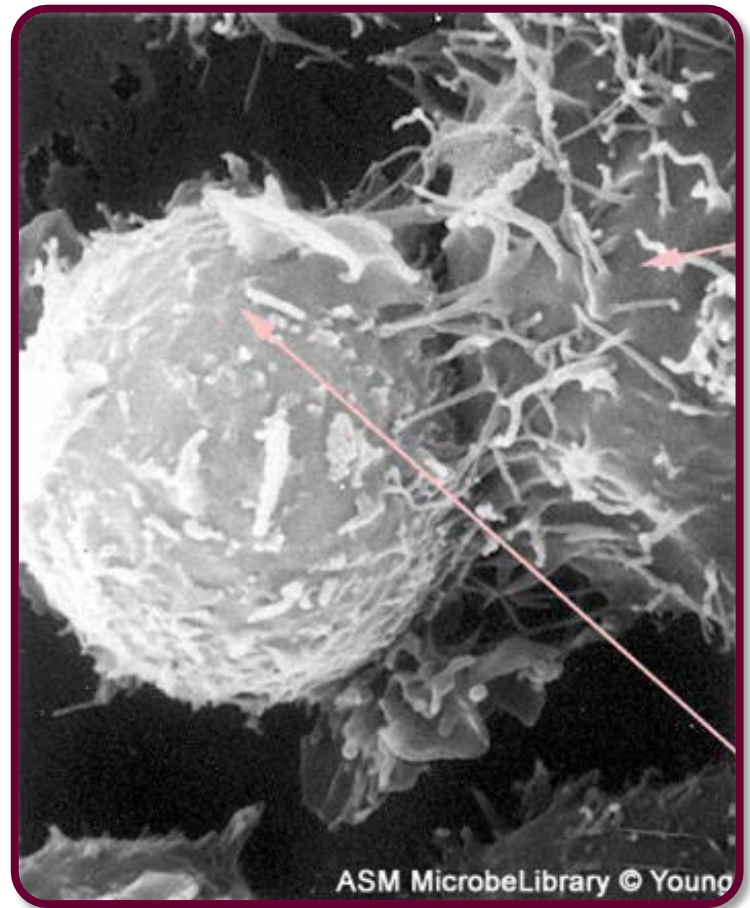


**Precise tumor targeting to cause cell death with range of technologies, including Antibody-Drug Conjugates**

# Empowering the Immune System to Fight Cancer

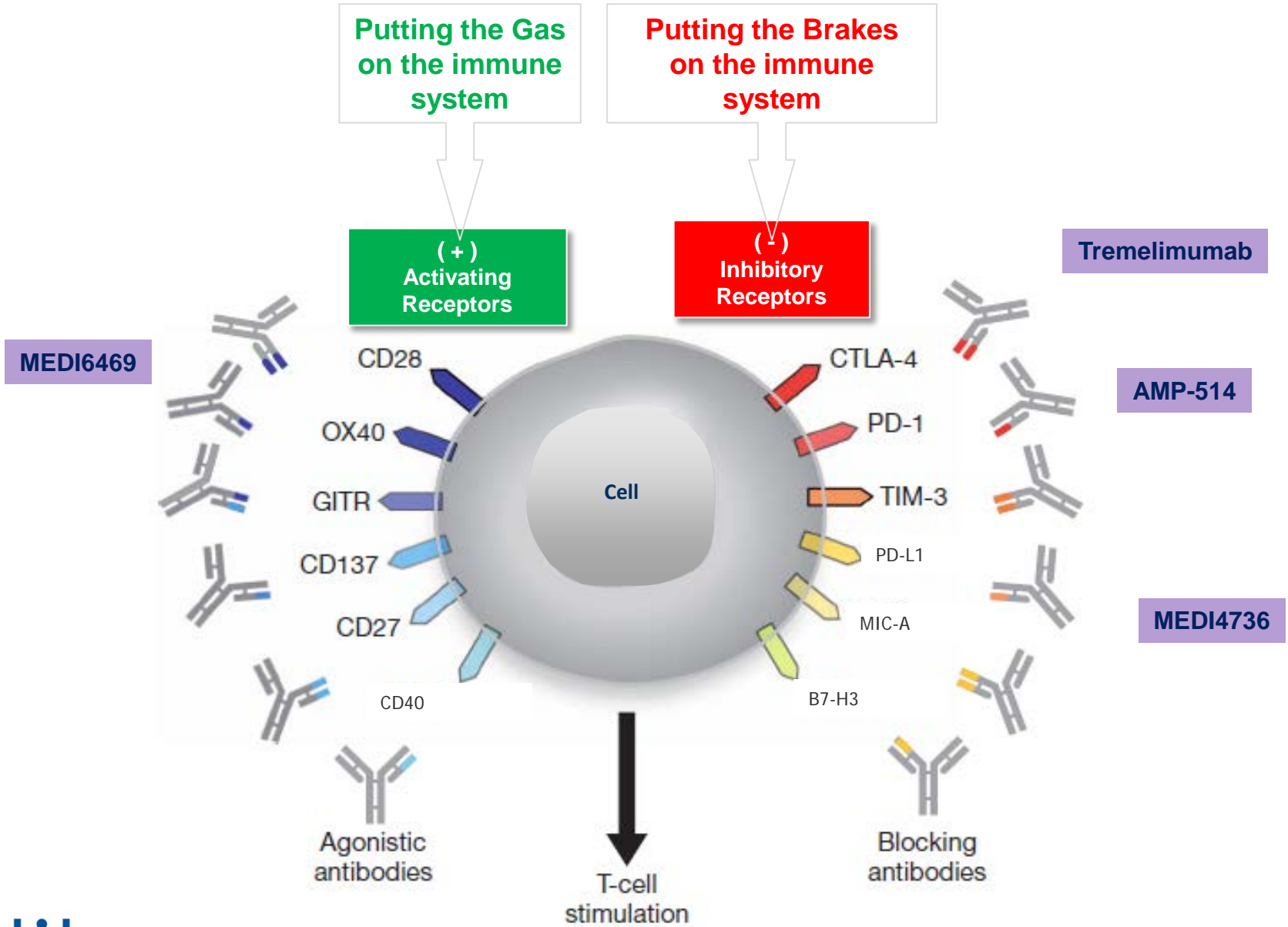
***“If we are ever going to use the word ‘cure’, the immune system is going to come into play.”***

Stephen Hodi, M.D., Dana-Farber, WSJ 6/14/11

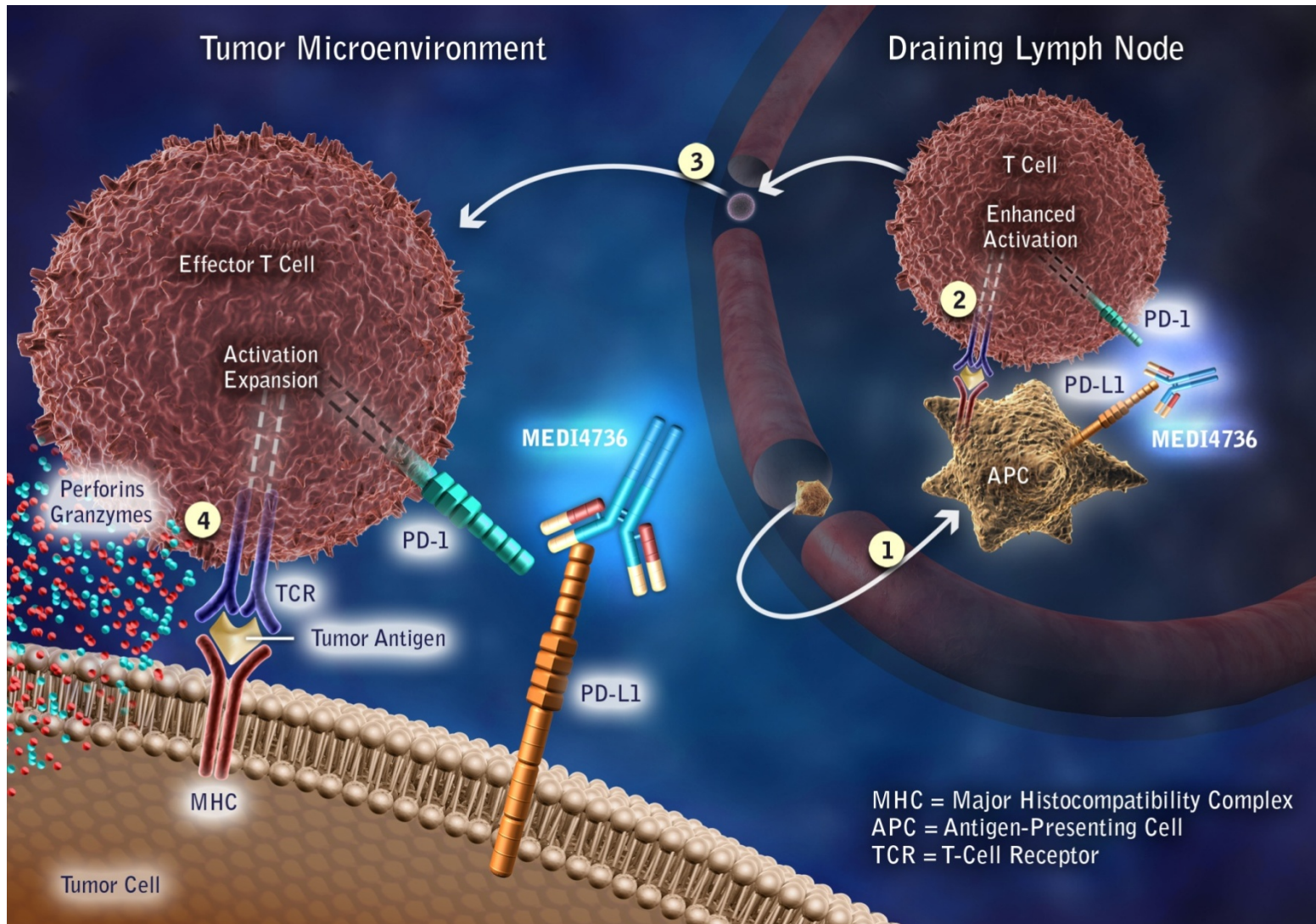




# Critical Checkpoints Hijacked by Cancer



# Spotlight: MEDI4736 or Anti-PD-L1 mAb



# How This Works



# IMT-C and IMT-C Combinations Are Now Clinically Validated

**BREAKING  
NEWS**

**ASCO 2011**

**APPROVAL OF FIRST ANTI-CTLA4 WITH IMPRESSIVE PROLONGED OS, IN MELANOMA**

**BREAKING  
NEWS**

**ASCO 2012**

**NEXT IMT PATHWAY VALIDATED: PD-1 EXTENDS ACTIVITY TO LUNG**

**BREAKING  
NEWS**

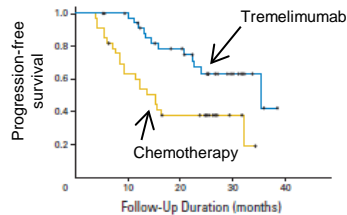
**ASCO 2013**

**SYNERGY OF PD-1 AND CTLA-4 DRAMATICALLY VALIDATED PRE-CLINICAL MODELS**

# Immune Therapy Portfolio Enables Novel Combinations

## Tremelimumab Anti-CTLA-4 mAb

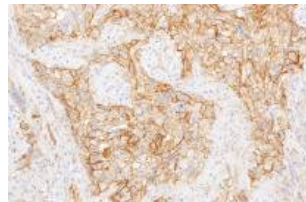
- Phase 2 in solid tumours
- Validated pathway
- Safety and efficacy data in >1,000 patients
- Focus on use in novel combinations



Phase 3 clinical trial in melanoma<sup>1</sup>

## MEDI4736 Anti-PD-L1 mAb

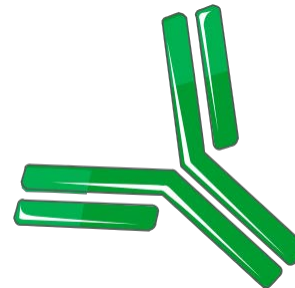
- Phase 1 in solid tumours
- Validated pathway in multiple tumour types
- Multiple Phase 1 to Phase 3 opportunities



PD-L1 expression in lung cancer<sup>2</sup>

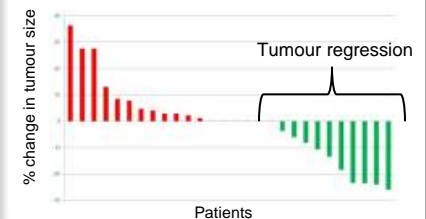
## AMP-514 Anti-PD-1 mAb

- Humanized, anti-PD-1 IgG4
- Mechanistically differentiated
- Late stage pre-clinical development



## MEDI6469 mOX40 agonist mAb

- Murine mAb in Phase 1 in solid tumours
- Clinical activity with single cycle in refractory patients
- First-in-class; follow on molecules will build on single agent and combination data



Phase 1 clinical trial<sup>3</sup>

<sup>1</sup> Ribas et al., J Clin Oncol 2013; 31:616-622

<sup>2</sup> Internal data

<sup>3</sup> Weinberg, AACR Tumor Immunology Conference Presentation, 2012

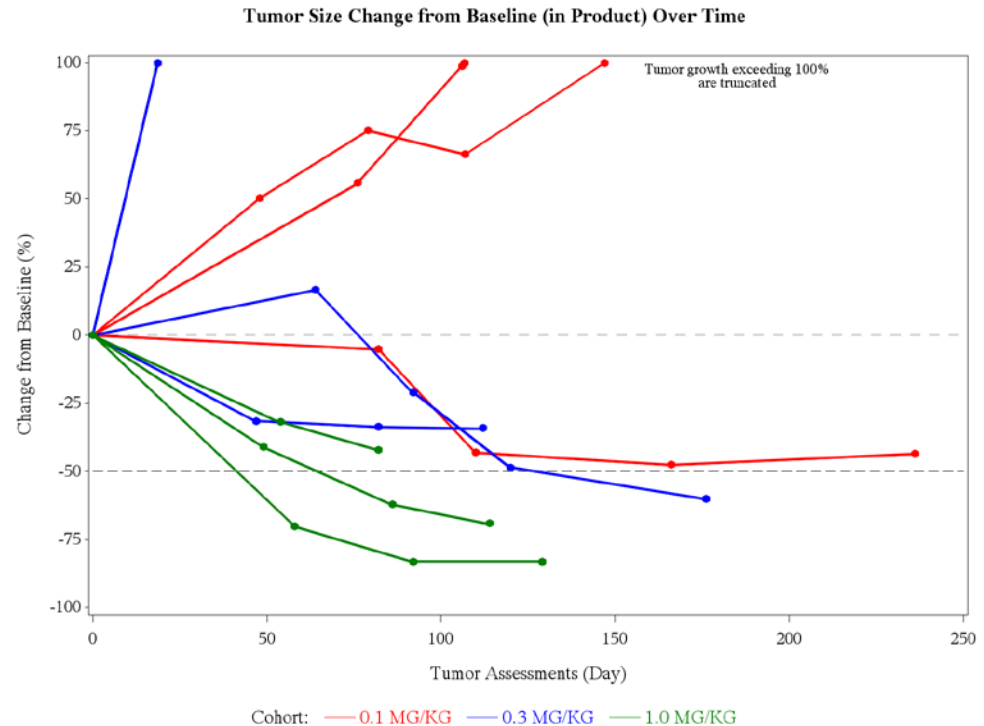
Multiple IMT-C pre-clinical programs provide additional combination opportunities

# MEDI4736 – Early Phase 1 Clinical Activity Observed

## Phase I Highlights

- Encouraging level of clinical activity in Phase 1 dose escalation with responses observed at lowest dose tested
- Early tumor shrinkage was observed across a range of doses
- Manageable safety profile, relative to the small data set

## Documented Clinical Evidence



\*Data as of 19Aug2013.

Note: Posttreatment CT scans not available for 2 patients (1 NSCLC patient each at 0.1 and 0.3 mg/kg).

NSCLC, non-small cell lung cancer.

n = 9

# IMT-C Development Plan Focused on Novel, Proprietary Combination Opportunities

	2013	2014		2015	
	H2	H1	H2	H1	H2
Monotherapy in new indications with favourable immune signature	■	■	■		
Novel IMT-C combinations: <ul style="list-style-type: none"> <li>• MEDI4736 (PD-L1) + Tremelimumab</li> <li>• CTLA-4 + mOX40</li> </ul>	■	■	■		
Other proprietary IMT-C combinations, including with AZ small molecules (e.g. IRESSA)	■	■	■		
IMT-C combinations with Standard of Care (e.g. chemotherapy, TKIs, RT)	■	■		■	

Registration enabling trials begin



TKI – tyrosine kinase inhibitor  
RT – radio therapy

■ Trials initiated    ■ Data read-outs begin

# The Power of a Combined Portfolio

AZ and MedImmune are uniquely positioned to combine agents within and between key scientific mechanisms

