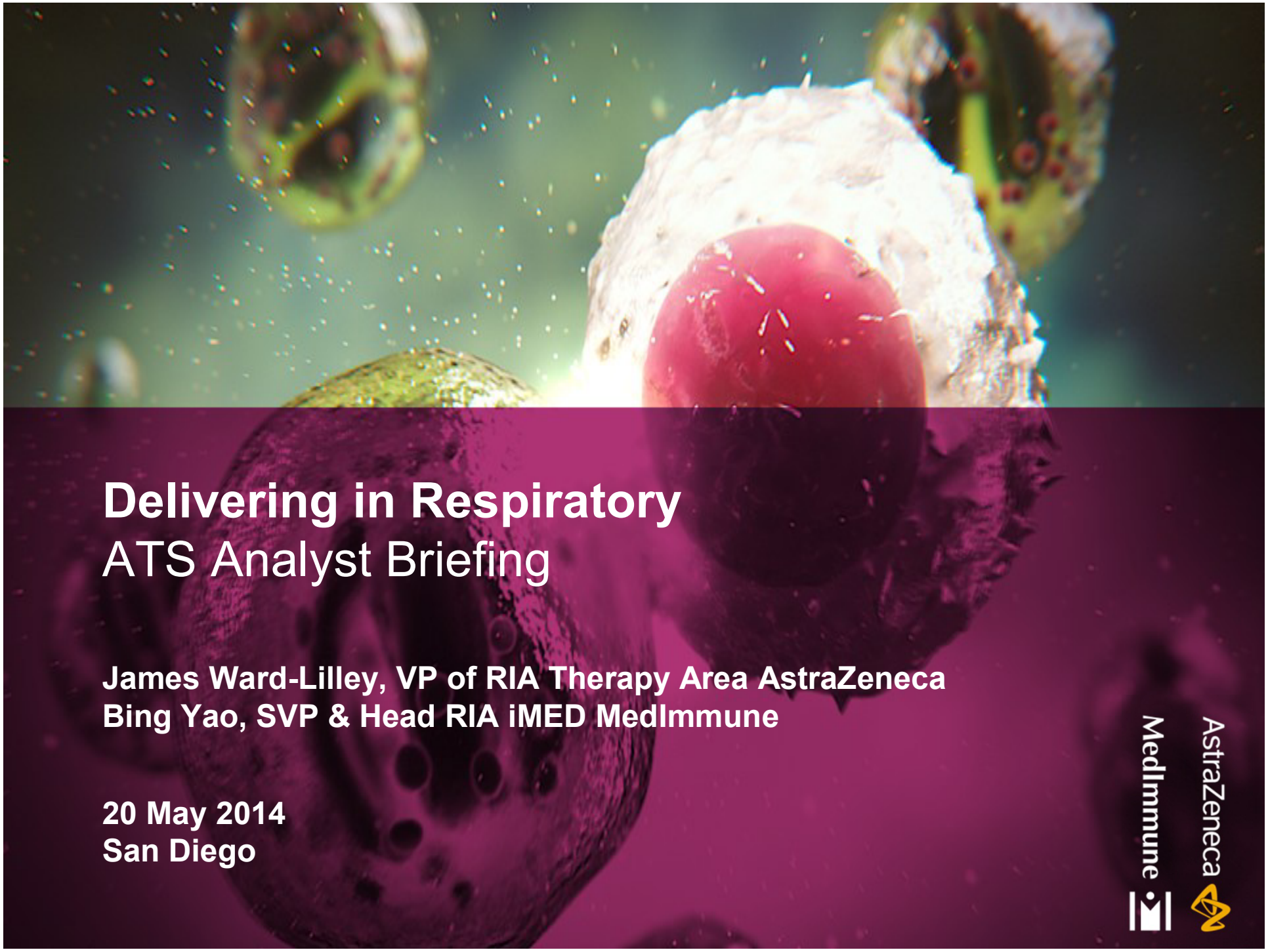


Delivering in Respiratory
ATS Analyst Briefing

James Ward-Lilley, VP of RIA Therapy Area AstraZeneca
Bing Yao, SVP & Head RIA iMED MedImmune

20 May 2014
San Diego

MedImmune
AstraZeneca

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 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; 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.

Respiratory panel

James Ward-Lilley
VP of RIA Therapy Area
AstraZeneca

Bing Yao
Head of MedImmune
RIA iMED

Chuck Bramlage
President, CEO
Pearl Therapeutics

Maarten Kraan
Head of RIA
Small Molecules
R&D iMED
AstraZeneca

Bill Mezzanotte
Head of RIA
Global Medicines
Development
AstraZeneca

Respiratory Strategy

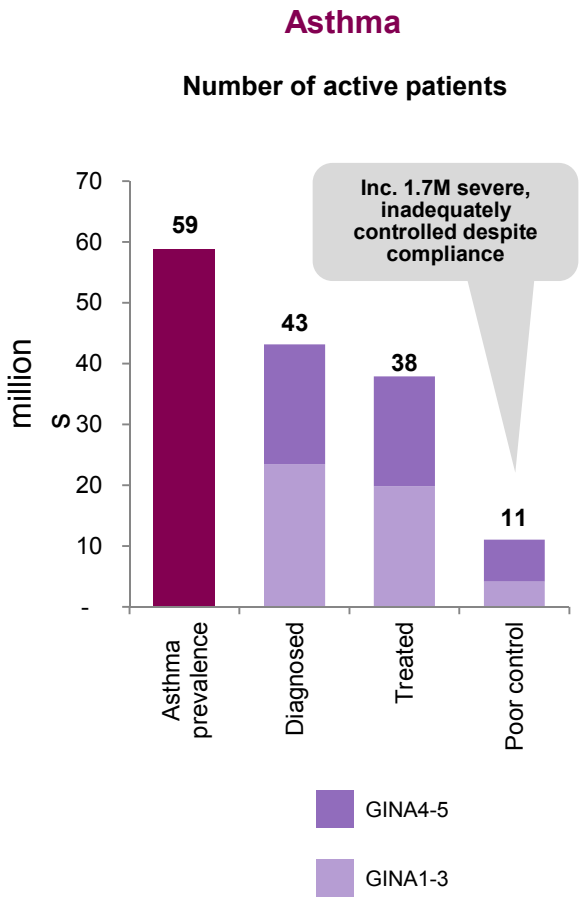
James Ward-Lilley, VP of RIA Therapy Area AstraZeneca

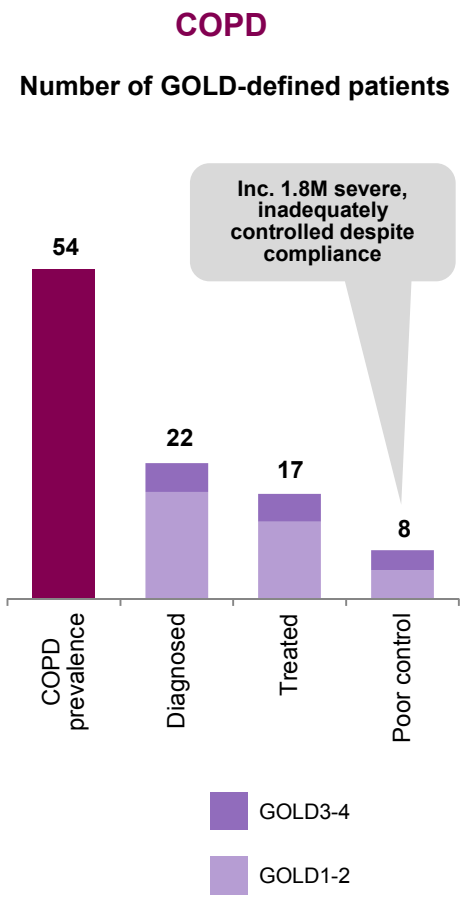
MedImmune

AstraZeneca


Our vision is to become an industry leader in innovative inhaled and targeted therapies for Asthma, COPD, and Idiopathic Pulmonary Fibrosis (IPF)
AstraZeneca
MedImmune

Significant unmet medical need remains in asthma and COPD





- Significant unmet need remains in both asthma and COPD
- Large numbers of patients remain uncontrolled despite treatment
- Diagnosis rates in COPD very low compared to asthma

Our Respiratory Strategy

1 Unique inhaled therapies

Symbicort® differentiation

Build differentiated inhaled range

Develop new devices and innovative product offerings

2 Innovation-driven targeted therapies

Introduce novel PHC-driven therapies

Expand therapeutic modalities

Understand patient phenotypes

3 Transform disease management

Evolve treatment paradigms

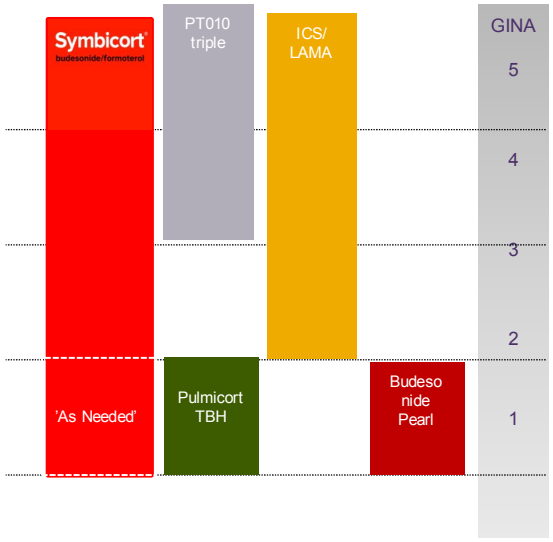
Understand biology and patient phenotypes

Offer step-changes in clinical outcomes

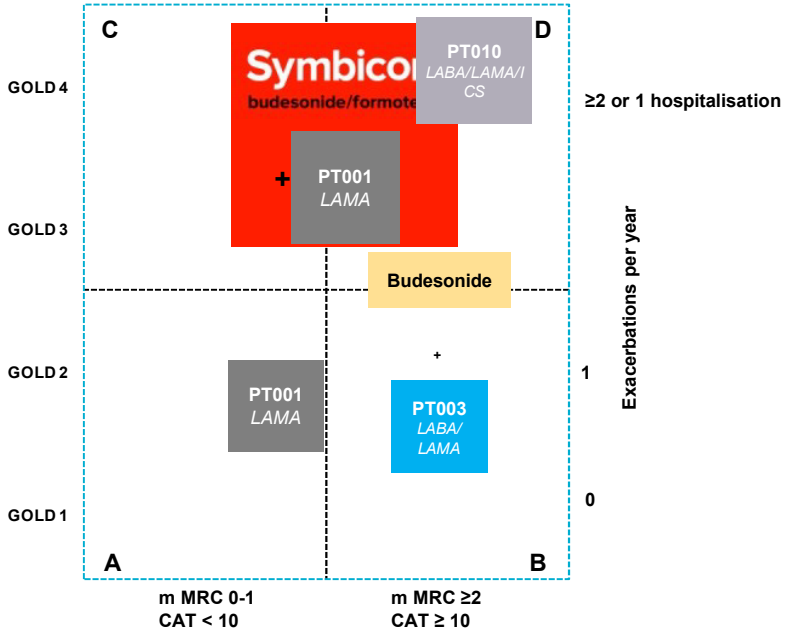
Pursue novel combinations to address heterogeneous biology

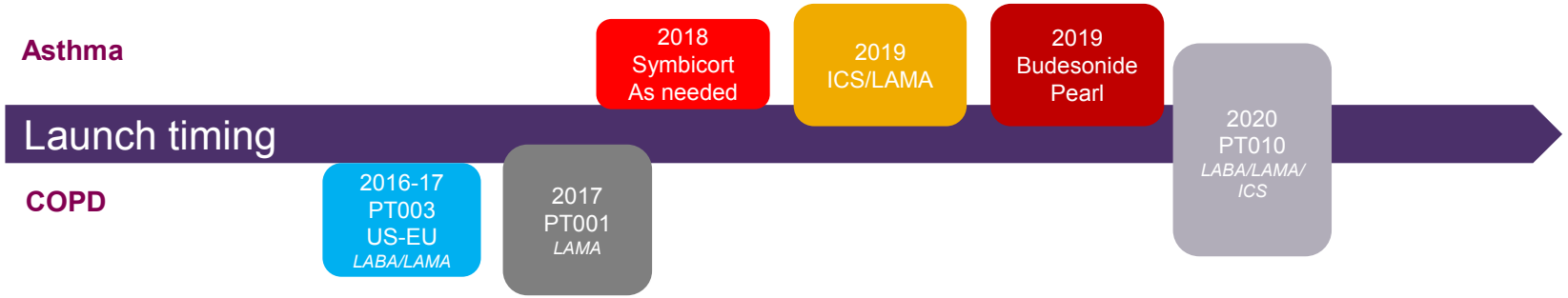
AZ unique inhaled portfolio potential: Clear positioning across the continuum of care

Asthma: GINA steps and treatment



COPD: GOLD patient segments and treatment





m MRC modified Medical Research Council dyspnea scale CAT COPD Assessment Test

AstraZeneca's Respiratory Pipeline

Phase I — 4 New Products

Small molecule

- **Inhaled TLR7 agonist**
  AZD8848
  asthma
- **Inhaled p38 inh**
  AZD7624
  COPD
- **CXCR2 antagonist**
  AZD4721
  COPD
- **TLR9**
  AZD1419
  asthma

Phase II — 6 New Products

Small molecule

- **CXCR2 antagonist**
  AZD5069
  asthma
- **MABA (dual)**
  AZD2115
  COPD
- **PT010**
  LABA/LAMA/ICS
  COPD

Biologic

- **benralizumab**
  IL-5R
  COPD
- **tralokinumab**
  IL-13
  asthma, IPF
- **brodalumab***
  IL-17R
  asthma
- **IL-1R**
  MEDI8968
  COPD
- **anti-TSLP***
  MEDI9929 / AMG 157
  asthma

Phase III — 3 New Products

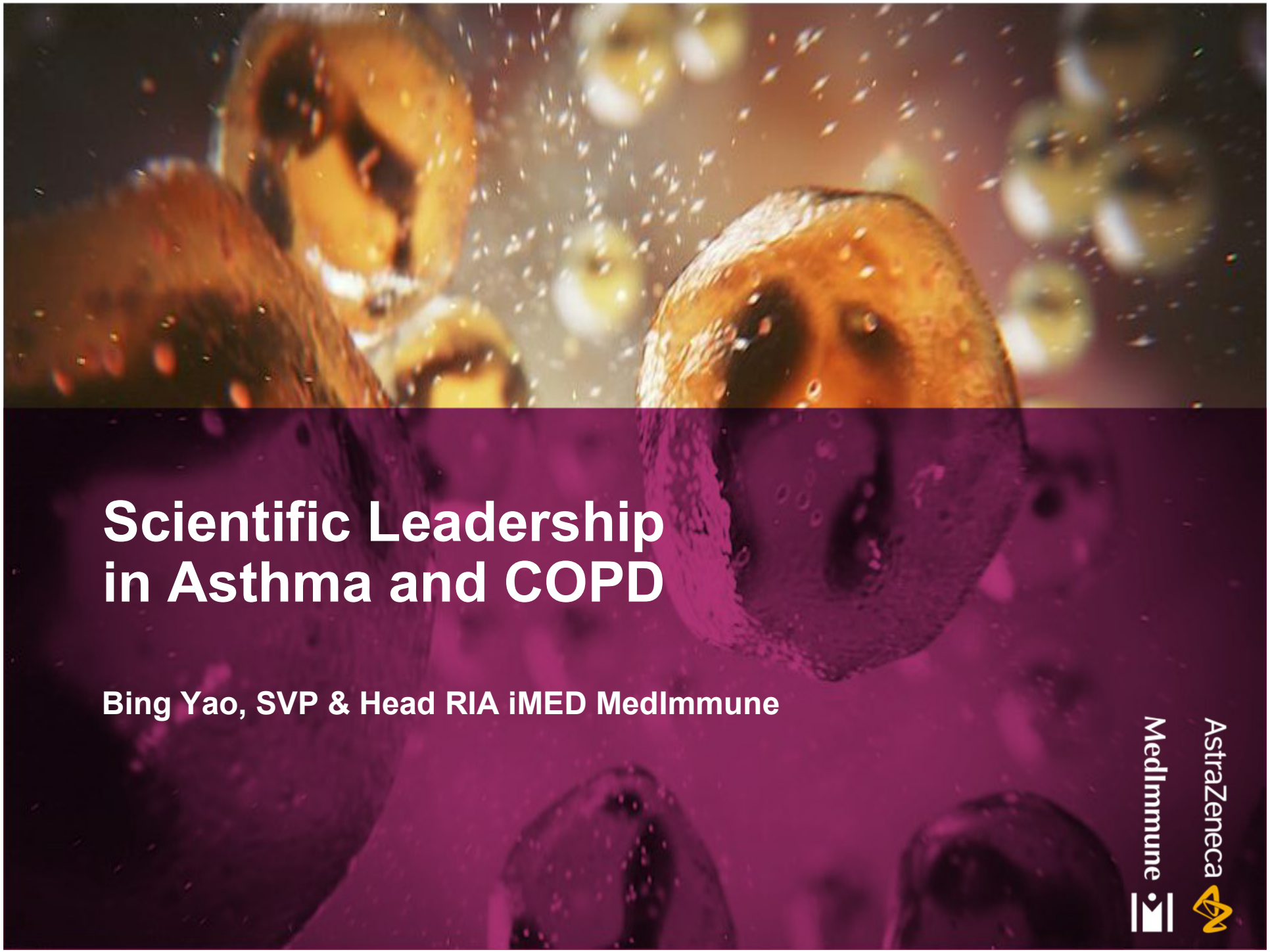
Small molecule

- **PT003**
  LABA/LAMA
  COPD
- **PT001**
  LAMA
  COPD

Biologic

- **benralizumab**
  IL-5R
  asthma

*Co-developed with Amgen / In phase III for psoriasis



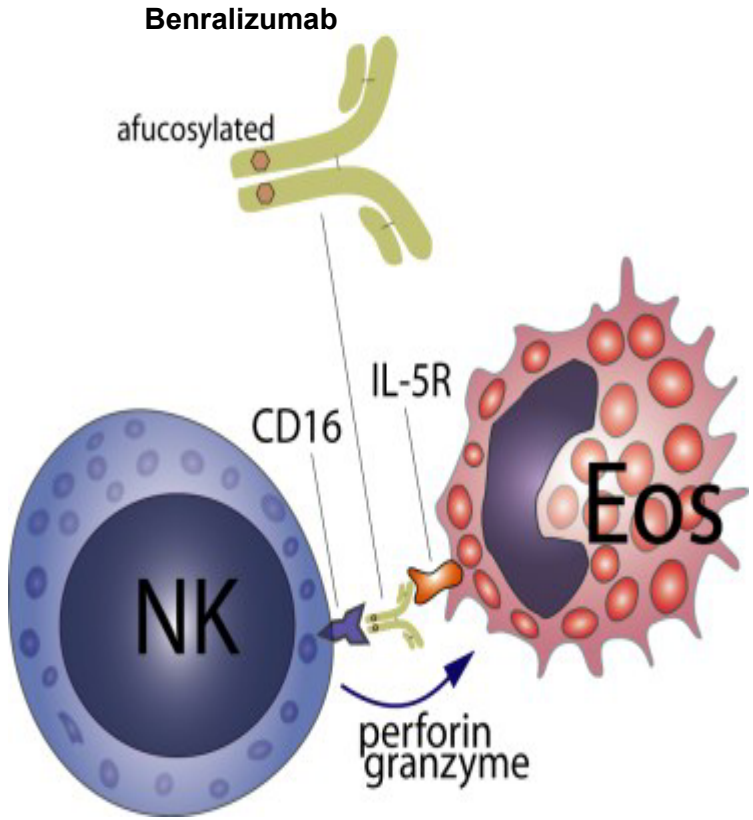
Scientific Leadership in Asthma and COPD

Bing Yao, SVP & Head RIA iMED MedImmune

AstraZeneca
MedImmune

Benralizumab in asthma: Potent anti-IL-5R antibody

Mechanism of Action: anti-IL-5Rα



~40-60% of severe asthmatics have eosinophilia*

Eosinophil count associated with exacerbation

Binds with high affinity to IL-5Rα and depletes eosinophils through Antibody-Dependent Cell-Mediated Cytotoxicity (ADCC)

* Internal data + Gibson Chest 2001, Dente AAAI 2006, Saha JACI 2008, and Wenzel Am J Respir Crit Care Med 1999

Benralizumab in eosinophilic asthma: Potential for best-in-disease profile

1 Unique MoA

The only IL-5 receptor targeting antibody

Potent depletion of target cells

2 Efficacy

Reduction in asthma exacerbations

Improvement in FEV_1

Improvement in ACQ-6 score

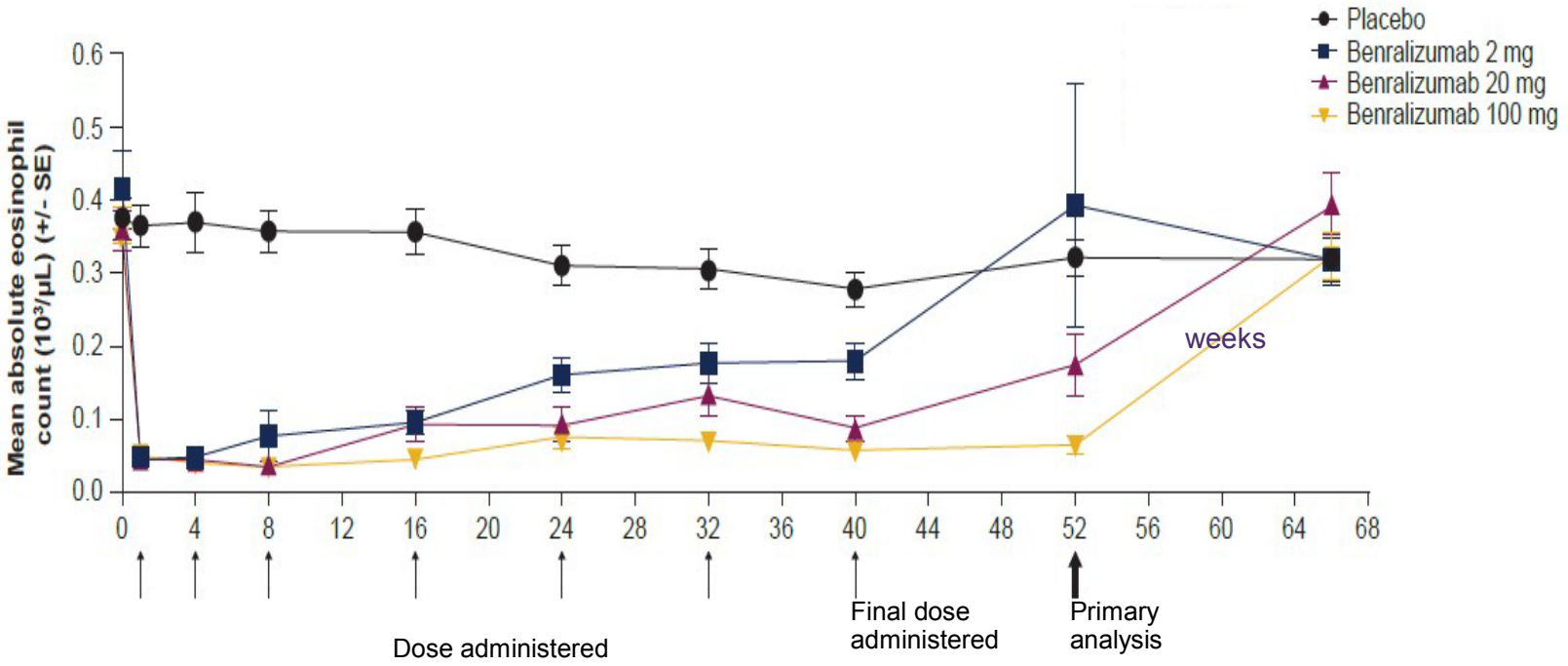
3 Dosing

Q4W/Q8W

FEV_1 – forced expiratory volume in 1 second ACQ-6 – asthma control questionnaire

Benralizumab: Eosinophil count reduction

Blood eosinophil count over time in eosinophilic subjects (mITT population)

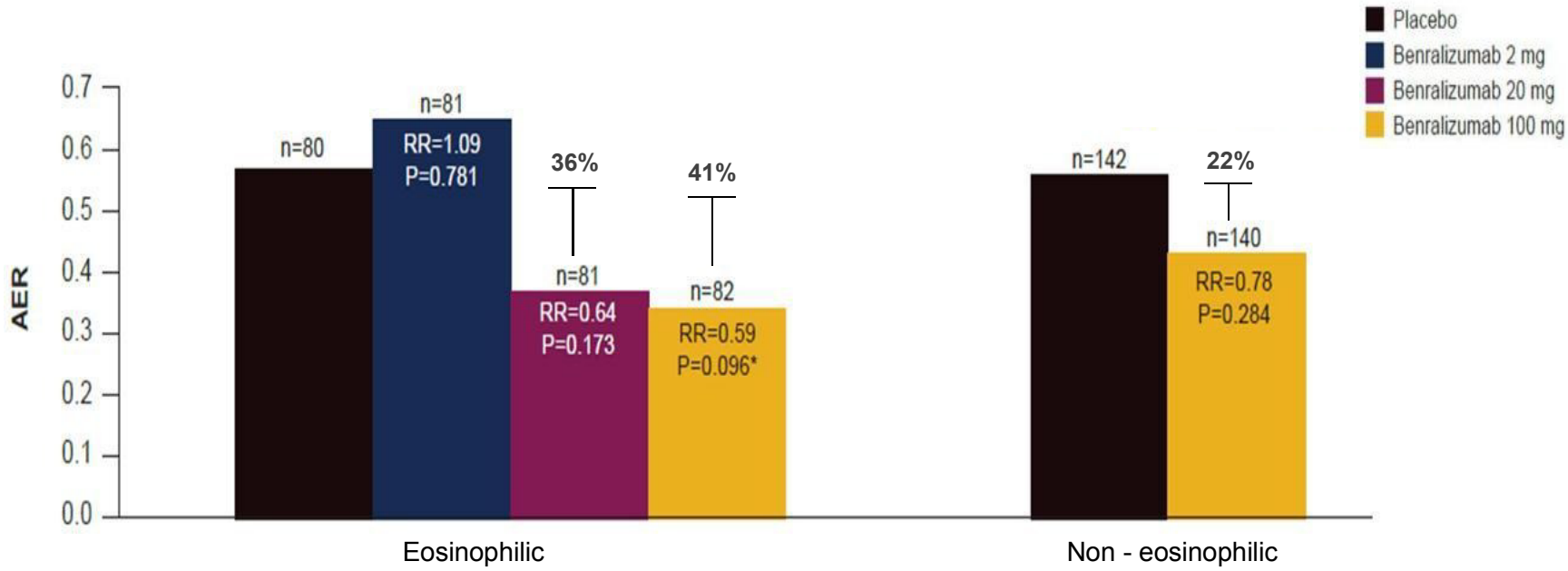


All doses of benralizumab decreased blood eosinophil counts to very low levels after first dose.

mITT – modified intent to treat

Benralizumab: Reduction in Asthma Exacerbation Rates (AER)

AER by eosinophil group (mITT population)

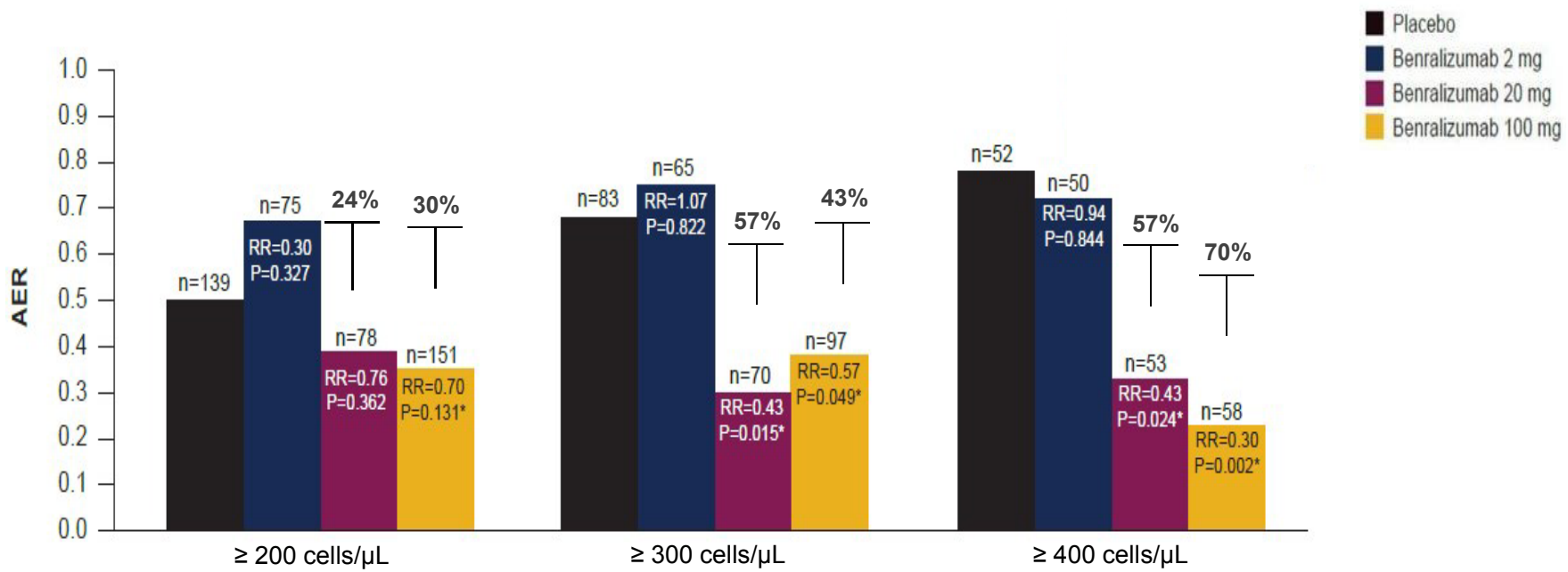


Met primary endpoint: In the eosinophilic group benralizumab 100 mg had a statistically significant reduction in AER compared with placebo

* P<0.169 vs. placebo is statistically significant
mITT – modified intent to treat; eosinophilic (ELEN Index positive and/or FENO ≥50 ppb);
ELEN Index is a probability-based algorithm based on peripheral blood eosinophils, lymphocytes, and neutrophils

Benralizumab: Reduction in Asthma Exacerbation Rates (AER)

AER by baseline eosinophil cut-off point (mITT population)

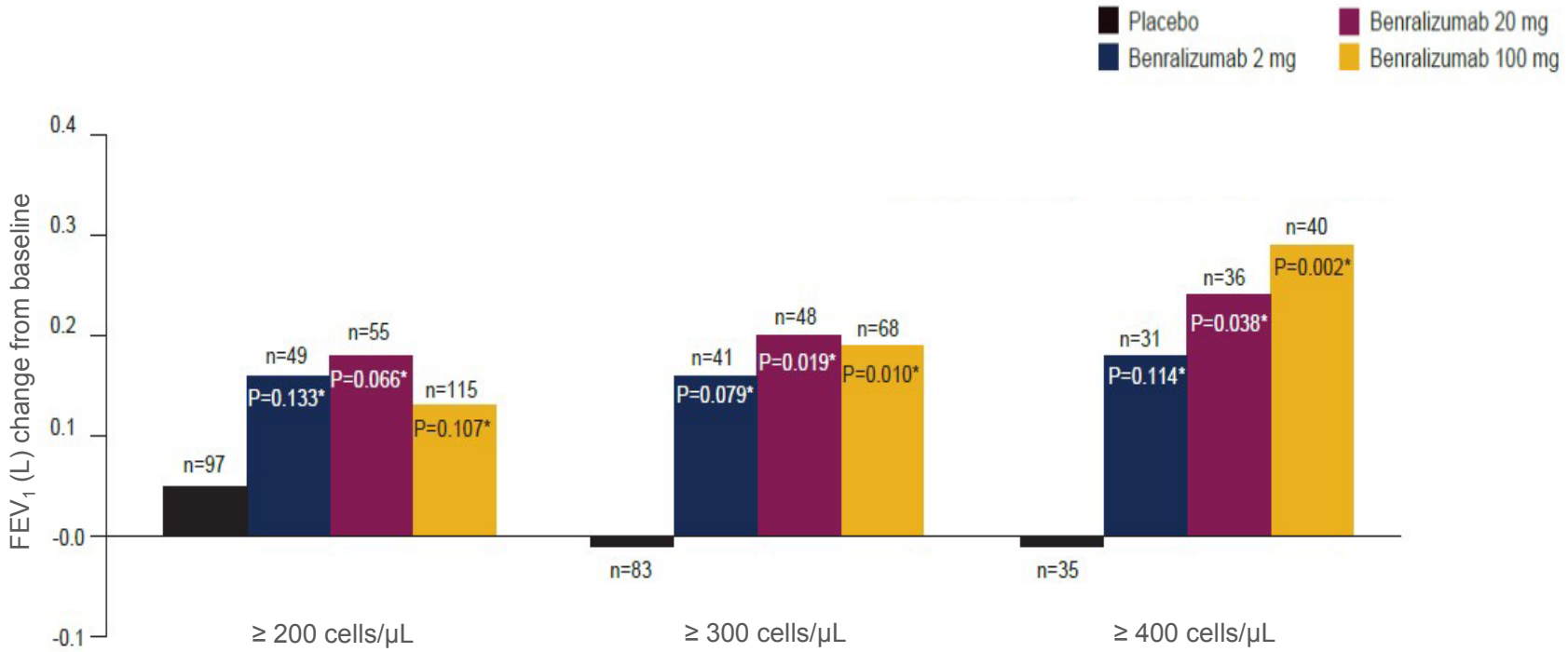


In the pre-specified subgroup analysis, benralizumab produced greater improvements as baseline blood eosinophil counts increased

*P<0.169 vs. placebo is statistically significant
•mITT – modified intent to treat

Benralizumab: Improvement in lung function

FEV_1 (L) change from baseline (mITT population)

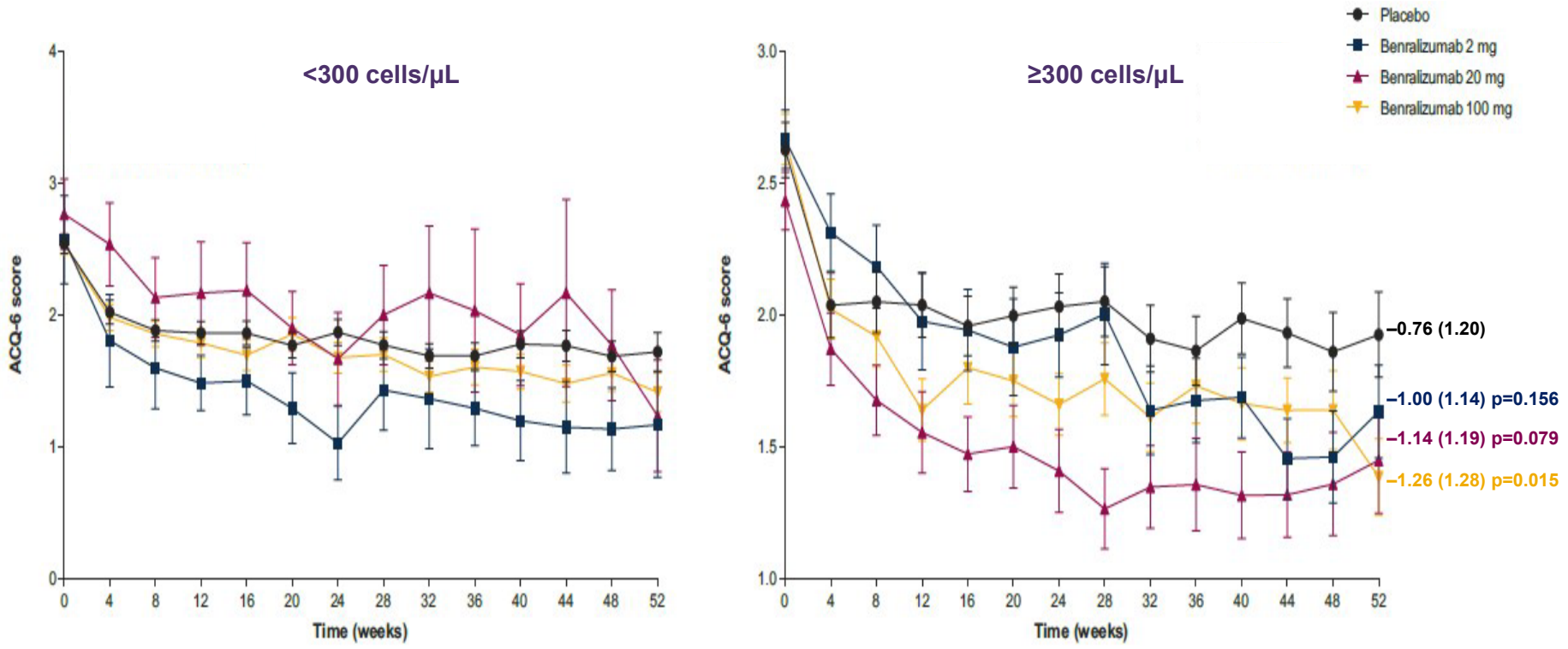


In subjects with blood eosinophil counts ≥200, ≥300 and ≥400 cells/µL, benralizumab resulted in significant improvement from baseline in FEV_1 (L) compared with placebo

mITT – modified intent to treat, FEV_1 – forced expiratory volume in 1 second

Benralizumab: Improvement in asthma control in patients with elevated eosinophils

ACQ-6 for baseline eosinophil (mITT population)



Significant improvements from baseline to Week 52 in mean ACQ-6 score for baseline blood eosinophil counts ≥300 cells/µL

mITT – modified intent to treat

Benralizumab Phase III asthma development plan

Two pivotal studies:

- Severe asthma uncontrolled on ICS/LABA therapies
- A range of blood eosinophil levels to fully characterize which patients may respond best to therapy
- Primary endpoint: Reduction in rate of exacerbations
- Secondary endpoints: Lung function (FEV_1) and symptoms (ACQ-6)

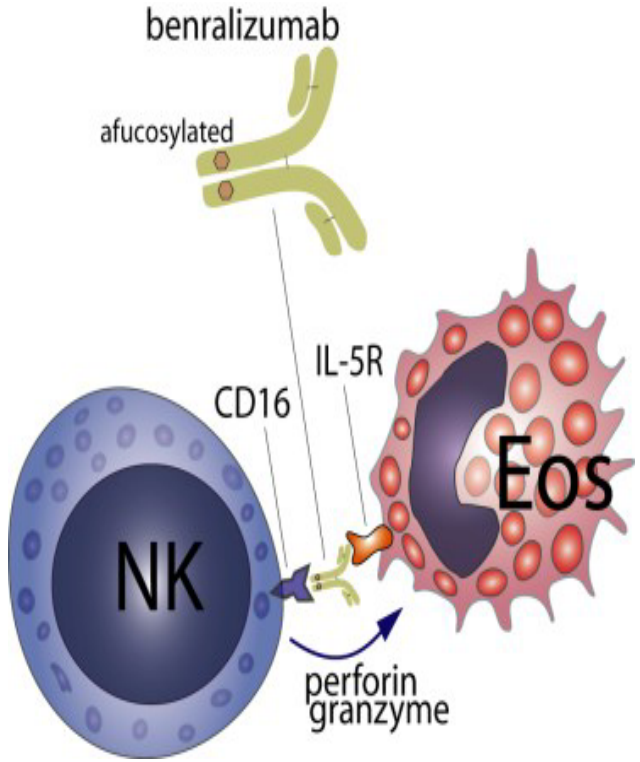
Phase III ongoing and on track to complete by 1Q 2016

A separate study will evaluate the effects of benralizumab on oral corticoid sparing

FEV_1 – forced expiratory volume in 1 second, ACQ – asthma control questionnaire

Benralizumab in COPD: Potent anti-IL-5R antibody

Mechanism of Action: anti-IL-5Rα



~30% of severe COPD patients have elevated blood eosinophils*

Elevated eosinophil count may be associated with increased exacerbations in this population

Binds with high affinity to IL-5Rα and depletes eosinophils through Antibody-Dependent Cell-Mediated Cytotoxicity (ADCC)

* Internal data

Benralizumab in COPD: Potential for best-in-class profile

1 Unique MoA

The only IL-5 receptor targeting antibody

Potent depletion of target cells

2 Efficacy

Significant improvement of FEV_1

Did not meet primary end in reduction of COPD exacerbations, however trend toward reduction with elevated EOS

Improvement in SGRQ-C total and symptom scores with elevated EOS

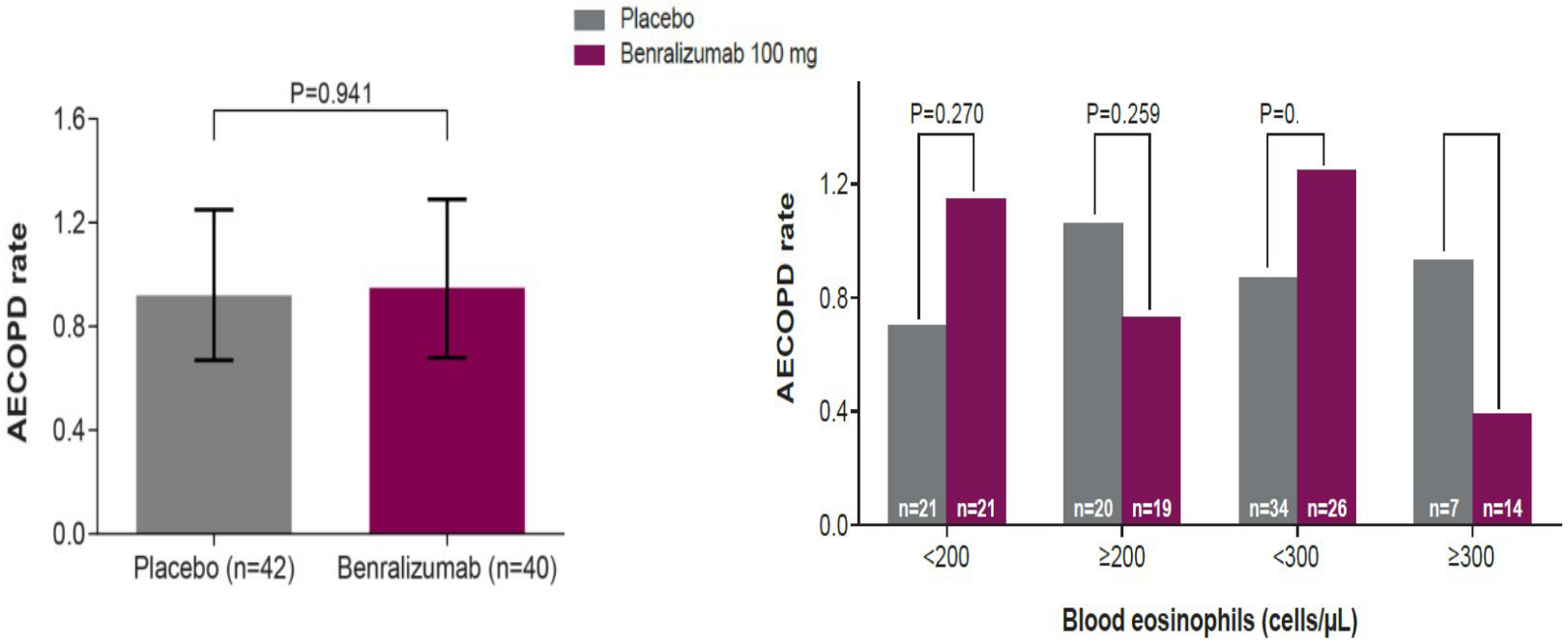
3 Dosing

Q4W/Q8W

FEV_1 – forced expiratory volume in 1 second, EOS – eosinophils, SGRQ-C – St. George's respiratory questionnaire COPD

Benralizumab phase 2a COPD results
Acute exacerbation rate

AECOPD rate for all-comers and by eosinophil group

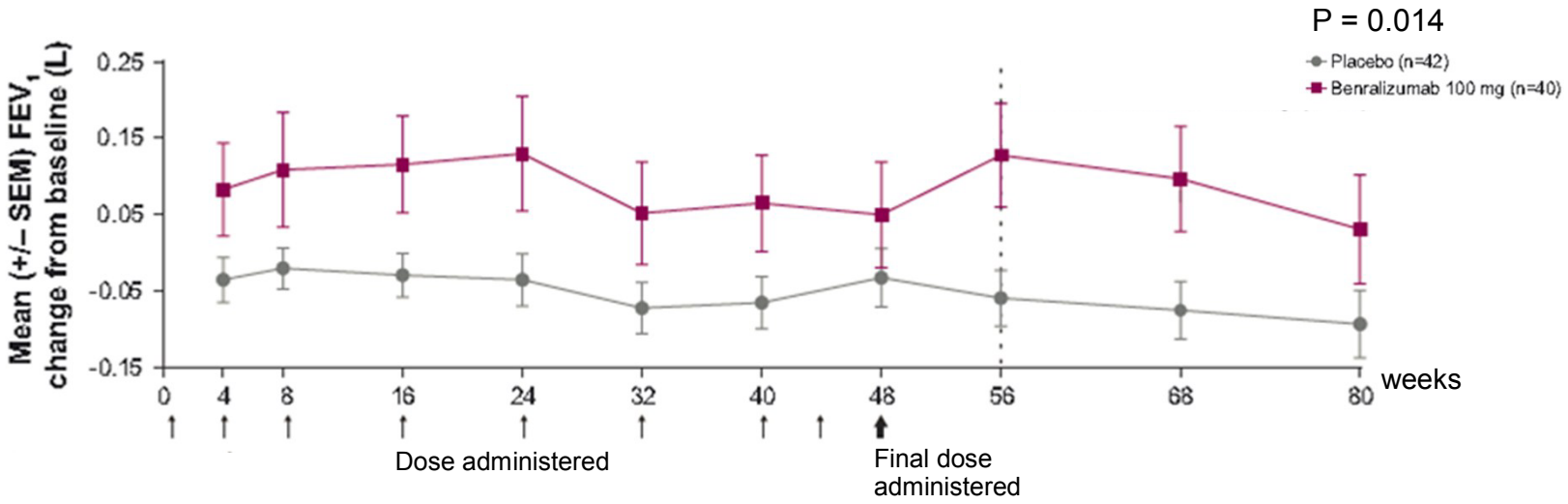


Primary Endpoint not met in overall population; however, reduction in AECOPD* rate for benralizumab with elevated eosinophils

*AECOPD = acute exacerbations of COPD

Benralizumab in COPD: Improvement in lung function

Mean change from baseline in FEV_1 over time (PP population)

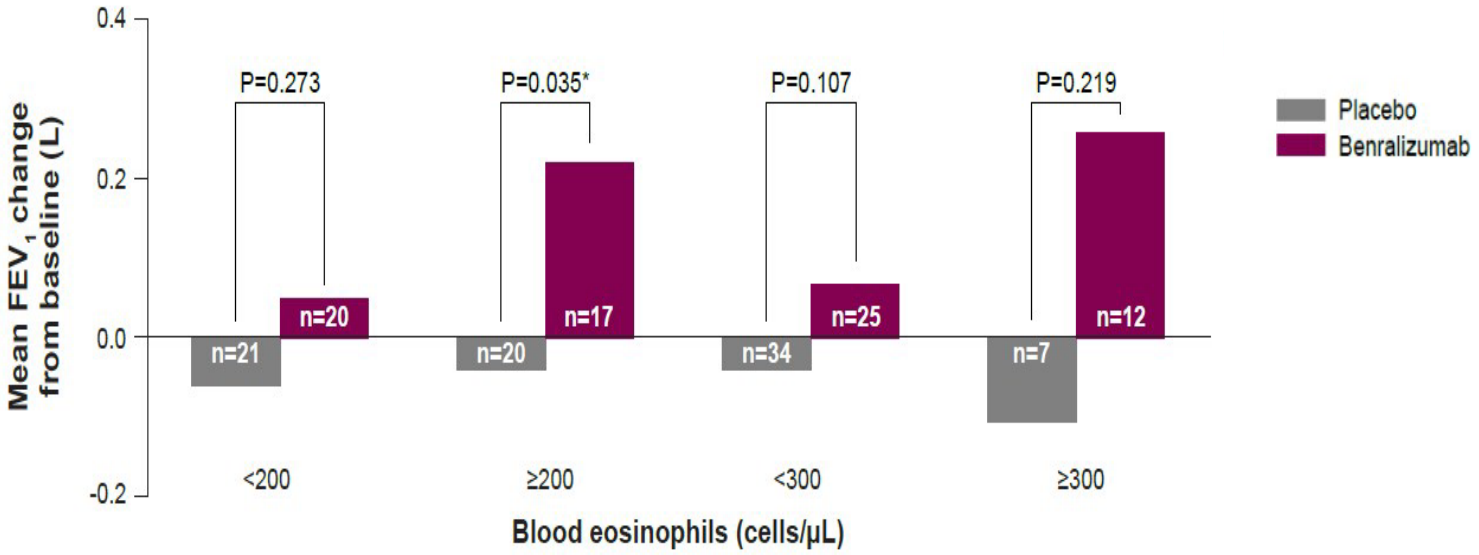


Improvement occurred after first dose and sustained

PP – per protocol, FEV_1 – forced expiratory volume in 1 second

Benralizumab in COPD: Improvement in lung function

Change from baseline to Week 56 in FEV_1 by baseline blood eosinophil count (PP population)



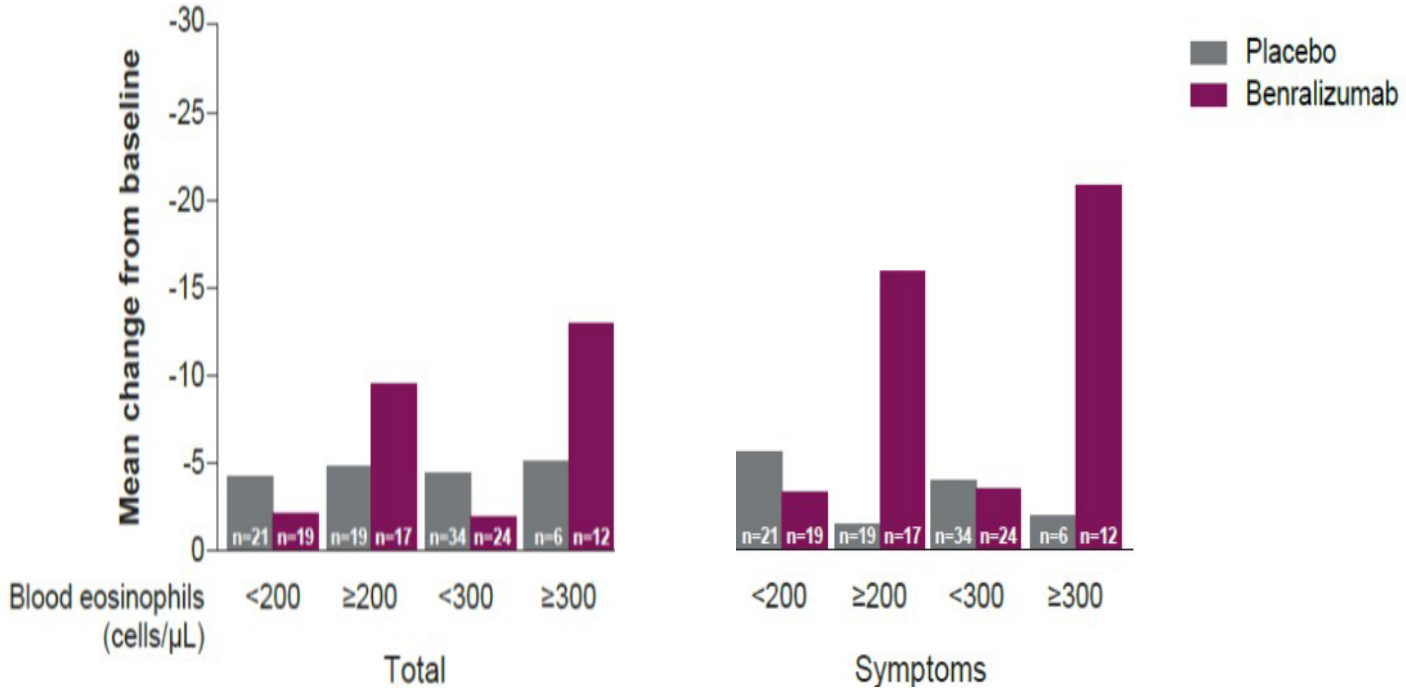
Significant improvements in FEV_1 through to Week 52 and improvement up to 32 weeks post last dose

* Statistically significant

PP – per protocol, FEV_1 – forced expiratory volume in 1 second

Benralizumab in COPD: Improvement in SGRQ-C score

Change from baseline to Week 56 in SGRQ-C total and symptom scores by baseline blood eosinophil count (PP population)



Greatest improvements in SGRQ-C total or symptom scores seen in patients with blood eos ≥200 and ≥300 cells/µL

PP – per protocol, SGRQ-C – St. George's respiratory questionnaire COPD

Benralizumab Phase III COPD development plan

Two pivotal studies:

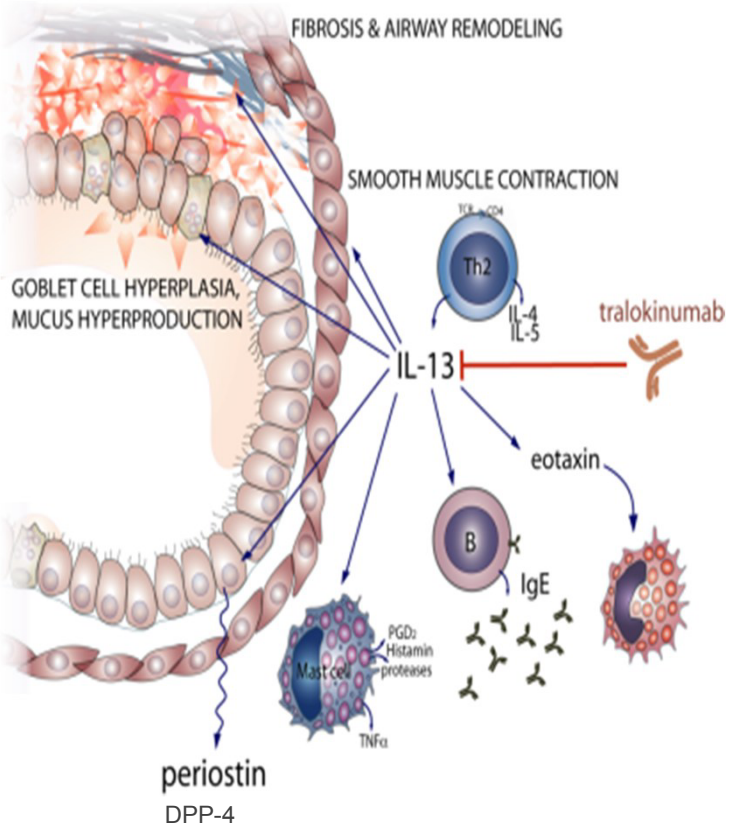
- Moderate to severe COPD patients with high exacerbation risk while receiving appropriate ICS/LABA/LAMA, ICS/LABA or LABA/LAMA therapies
- Trial includes patients with a range of blood eosinophil levels to fully characterize which patients may respond best to therapy
- Primary endpoint: Reduction in rate of exacerbations
- Secondary endpoints: Lung function (FEV_1) and health-related quality of life (SGRQ)

Phase III start planned for 3Q 2014

FEV_1 – forced expiratory volume in 1 second, SGRQ-C – St. George's respiratory questionnaire COPD

Tralokinumab (anti-IL-13) for severe uncontrolled asthma

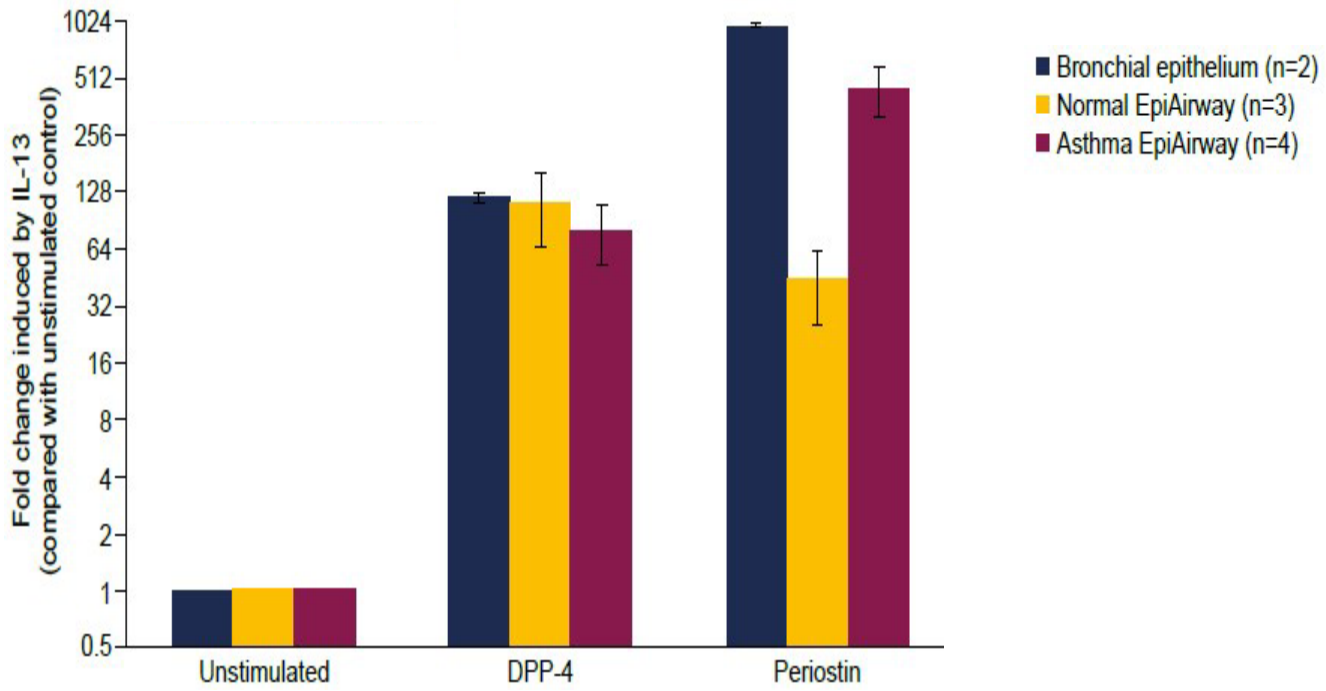
Mechanism of Action: anti-IL-13



- Human antibody blocking IL-13 – a central mediator of asthma
- Potential biomarkers to target treatment and optimise measures of asthma control
- Asthma Phase III start expected 3Q2014
- IPF Phase II ongoing

Hypothesis that tralokinumab has enhanced activity with elevated IL-13 pathway activation

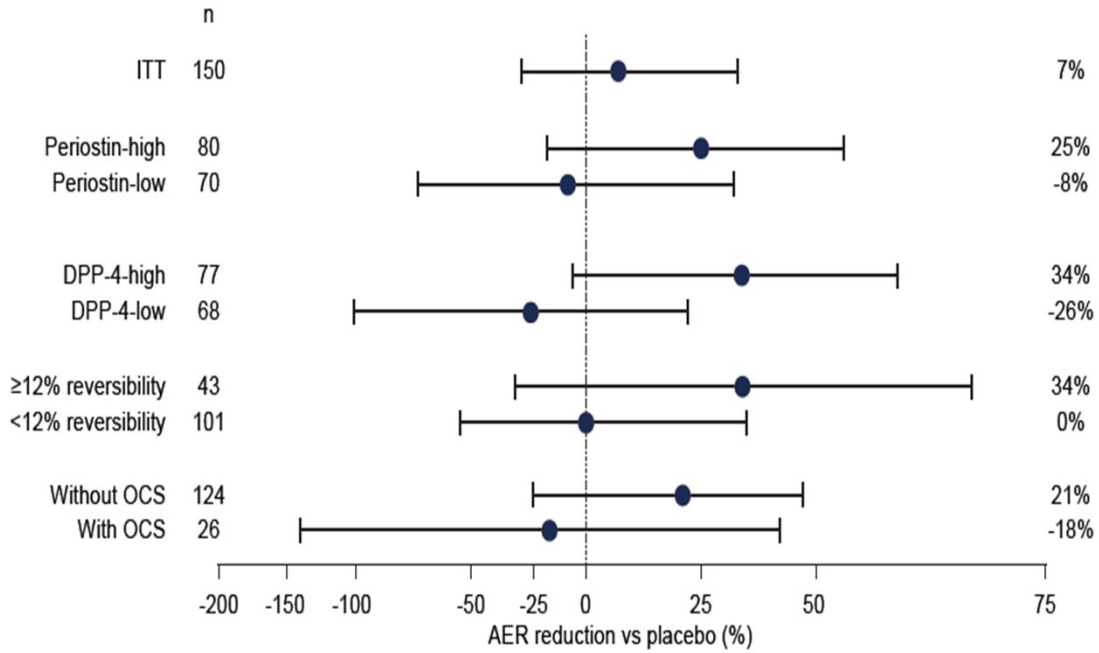
DPP-4 and periostin expression levels in lung epithelial cells after IL-13 stimulation



IL-13 stimulation increases periostin and DPP-4 expression in lung epithelial cells, with potential as surrogate biomarkers for IL-13 pathway activation in uncontrolled asthma

Tralokinumab: Effect on Asthma Exacerbation Rates (AER)

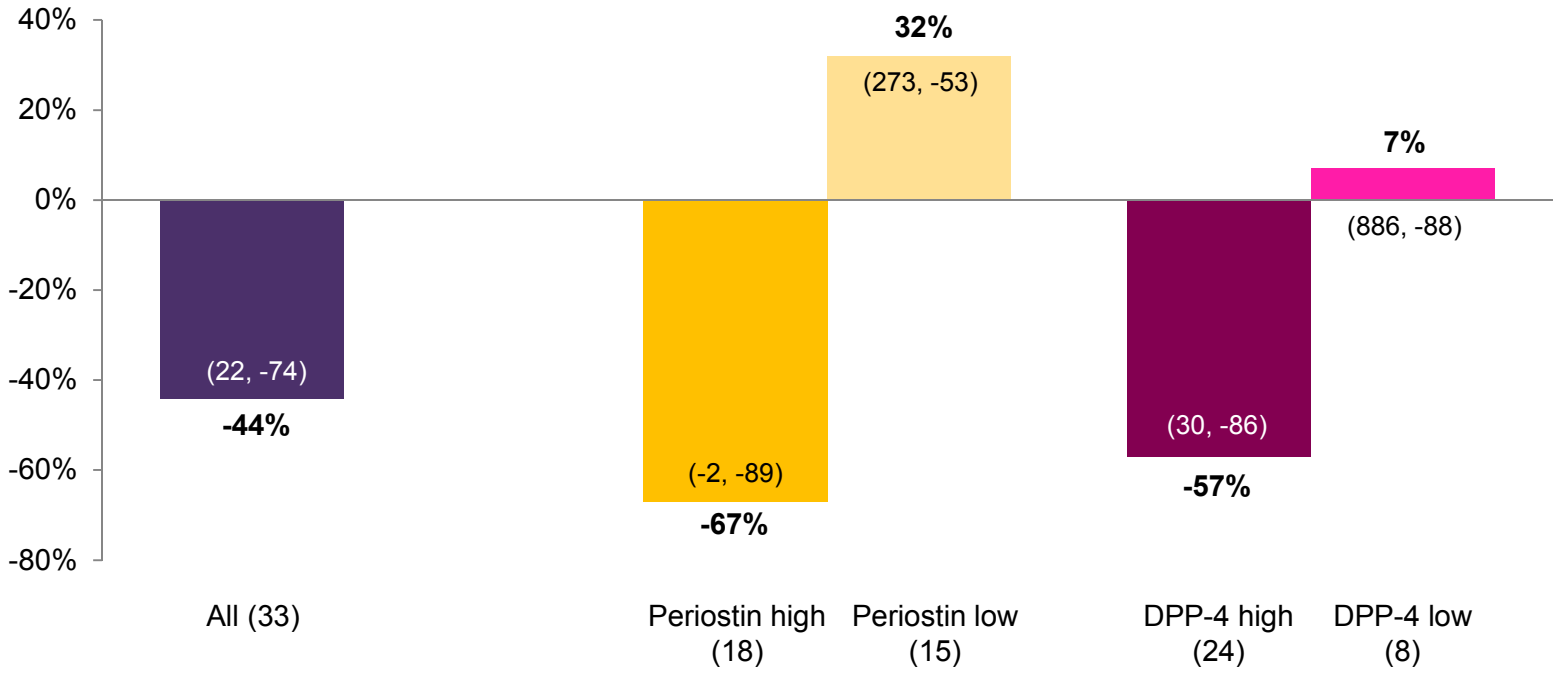
Percentage AER reduction (95% CI) for tralokinumab 300 mg Q2W vs placebo at Week 52 (subgroup analyses)



Trends towards greater AER reduction vs placebo in periostin-high and DPP-4-high subgroups, and subjects responsive to bronchodilators and not receiving chronic OCS

Tralokinumab: Effect on Asthma Exacerbation Rates (AER)

AER for tralokinumab 300 mg Q2W vs placebo at Week 52

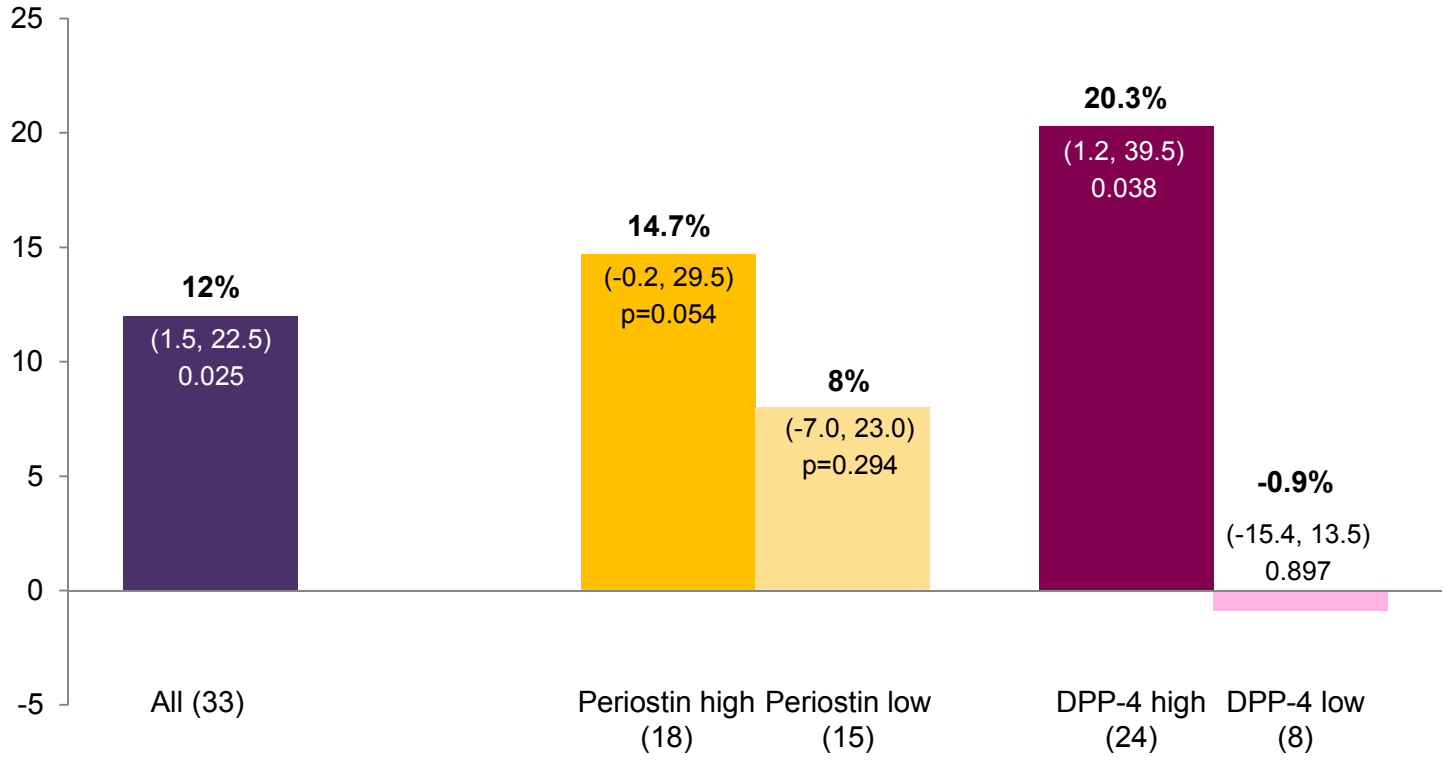


Enhancement of AER reduction with higher levels of serum periostin or DPP-4 in an exploratory subgroup of subjects responsive to bronchodilators and not receiving chronic OCS

Periostin high and DPP-4 high defined by serum levels ≥median at randomization

Tralokinumab: Improvement in lung function in periostin-high patients*

FEV_1 % change from baseline (net of placebo)



Enhancement of effect of FEV_1 with higher levels of serum periostin or DPP-4 in an exploratory subgroup of subjects responsive to bronchodilators and not receiving chronic OCS

*Q2W reversible without OCS use FEV_1 – forced expiratory volume in 1 second
Periostin high and DPP-4 high defined by serum levels ≥median at randomization

Tralokinumab Phase IIb asthma results Secondary endpoints

Tralokinumab 300 mg (Q2W reversible without OCS use)

Secondary endpoints difference from placebo	All (n=33)	Periostin-high (n=18)	Periostin-low (n=15)	DPP-4-high (n=24)	DPP-4-low (n=8)
ACQ-6 change from baseline	**-0.55**	**-0.68**	**-0.23**	**-0.89**	**-0.43**
(95% CI)	(-1.07, -0.04)	(-1.31, -0.06)	(-1.10, 6.4)	(-1.63, -0.14)	(-1.41, 0.56)
P-value	0.036	0.033	0.596	0.020	0.390
AQLQ(S) change from baseline	**0.70**	**0.64**	**0.71**	**1.26**	**0.24**
(95% CI)	(0.12, 1.28)	(-0.11, 1.39)	(-0.23, 1.65)	(0.18, 2.04)	(-0.87, 1.35)
P-value	0.019	0.095	0.138	0.002	0.663

Enhancement of effect of ACQ-6 and AQLQ(s) with higher levels of serum periostin or DPP-4 in an exploratory subgroup of subjects responsive to bronchodilators and not receiving chronic OCS

Periostin high and DPP-4 high defined by serum levels ≥median at randomization

FEV_1 – forced expiratory volume in 1 second, ACQ-6 – asthma control questionnaire, AQLQ – asthma quality of life questionnaire

Tralokinumab in asthma

1 Novel biomarker

Periostin and DPP-4: promising IL-13 surrogate biomarkers for PHC approach

2 Efficacy

Improvements across a range of asthma control measures observed in Phase IIb subgroups (AER, FEV_1, ACQ and AQLQ)

3 Target Population

Phase III will confirm the population that will optimally benefit from tralokinumab therapy

AER – Asthma exacerbation rates; FEV_1 – forced expiratory volume in 1 second, ACQ - Asthma Control Questionnaire
AQLQ - Asthma Quality of Life Questionnaire

Tralokinumab Phase III asthma development plan

Two pivotal studies:

- Phase III design and patient population builds on learning from the Phase II program
- Focus will be on the 300mg Q2W dosing schedule and confirming patient biomarker selection criteria
- Primary endpoint: Reduction in rate of exacerbations
- Secondary endpoints: Lung function (FEV_1) and symptoms (ACQ-6)

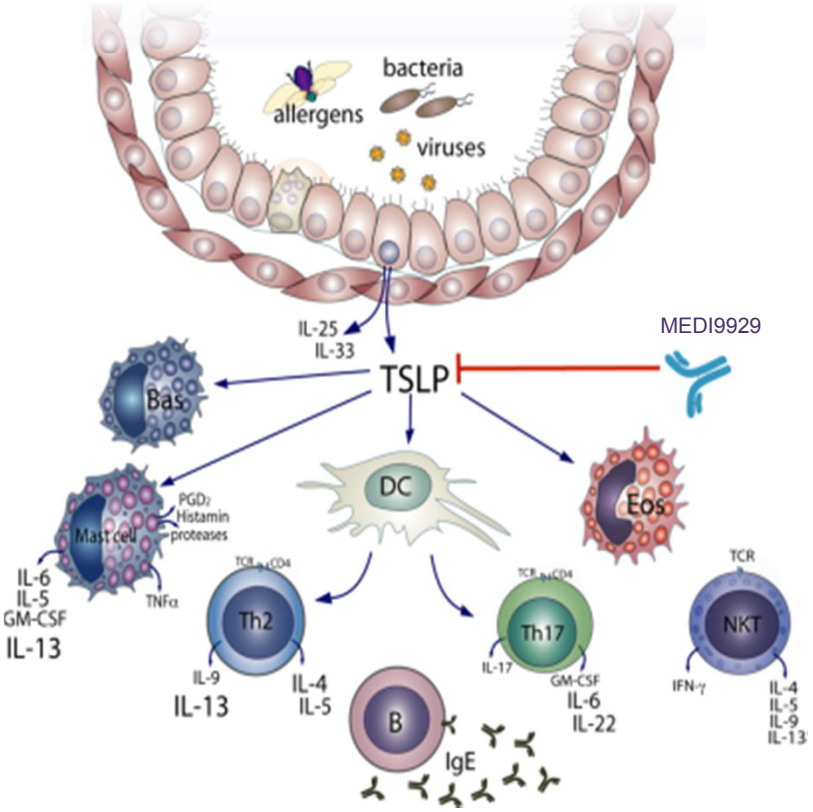
Phase III start planned for 3Q 2014

Oral corticosteroid sparing will also be included in the program

FEV_1 – forced expiratory volume in 1 second, ACQ – asthma control questionnaire

Anti-TSLP* (MEDI9929/AMG 157)

Mechanism of Action: anti-TSLP



- Strong allergen challenge data (Phase Ib)
- Decreased EAR & LAR
- Decreased blood and sputum eosinophils
- Reduced FENO

* Co-developed with Amgen; EAR - Early asthmatic response; LAR - Late asthmatic response; FENO - Fractional exhaled nitric oxide

Anti-TSLP* (MEDI9929/AMG 157) data published in NEJM today

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effects of an Anti-TSLP Antibody on Allergen-Induced Asthmatic Responses

Gail M. Gauvreau, Ph.D., Paul M. O'Byrne, M.B., Louis-Philippe Boulet, M.D., Ying Wang, Ph.D., Donald Cockcroft, M.D., Jeannette Bigler, Ph.D., J. Mark FitzGerald, M.D., Michael Boedigheimer, Ph.D., Beth E. Davis, Ph.D., Clapton Dias, Ph.D., Kevin S. Gorski, Ph.D., Lynn Smith, Ph.D., Edgar Bautista, B.S., Michael R. Comeau, B.S., Richard Leigh, M.B., Ch.B., Ph.D., and Jane R. Parnes, M.D.

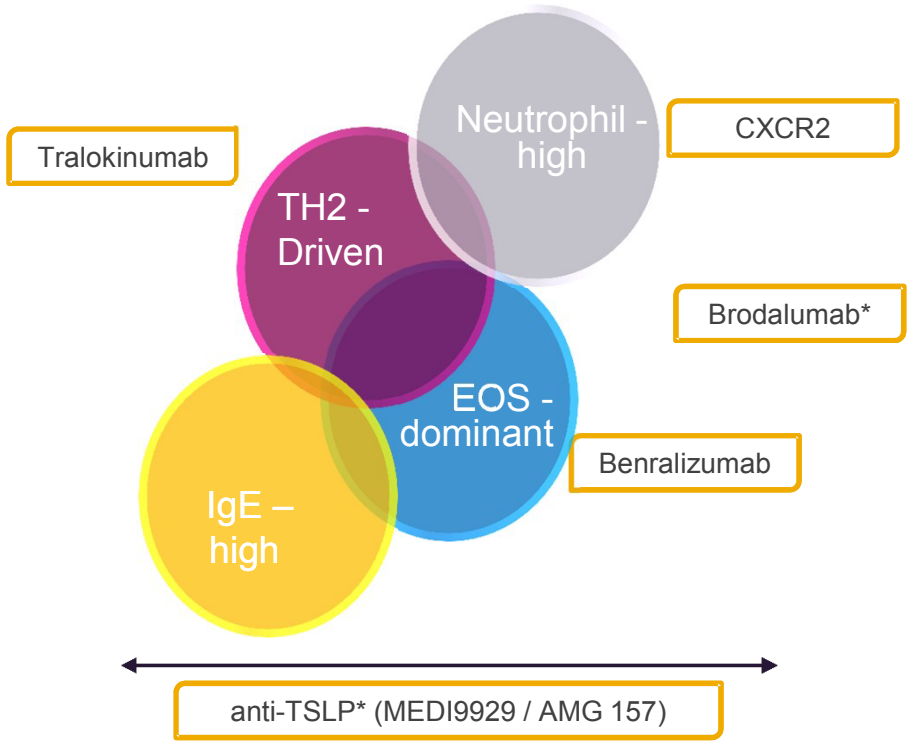
CONCLUSIONS

Treatment with AMG 157 reduced allergen-induced bronchoconstriction and indexes of airway inflammation before and after allergen challenge. These findings are consistent with a key role for TSLP in allergen-induced airway responses and persistent airway inflammation in patients with allergic asthma. Whether anti-TSLP therapeutics will have clinical value cannot be determined from these data. (Funded by Amgen; ClinicalTrials.gov number, NCT01405963.)

Phase II Study in Severe Asthma is Recruiting

*Co-developed with Amgen

Severe asthma: Potential to transform disease management by targeting distinct patient subsets



Asthma: Highly heterogeneous disease

- Developing understanding of underlying cause
- Studying patient sub-types
- Developing diagnostics
- Tailoring therapies

*Co-developed with Amgen

Q&A

James Ward-Lilley
VP of RIA Therapy Area
AstraZeneca

Bing Yao
Head of MedImmune
RIA iMED

Chuck Bramlage
President, CEO
Pearl Therapeutics

Maarten Kraan
Head of RIA
Small Molecules
R&D iMED
AstraZeneca

Bill Mezzanotte
Head of RIA
Global Medicines
Development
AstraZeneca

Delivering in Respiratory
ATS Analyst Briefing

20 May 2014
San Diego

MedImmune
AstraZeneca