AstraZeneca
What science can do

Investor science conference call
European Respiratory Society

07 September 2016

Forward-looking statements

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This document contains certain forward-looking statements with respect to the operations, performance and financial condition of the Group, including, among other things, statements about expected revenues, margins, earnings per share or other financial or other measures. 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 document 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, or limitations to, patents, marketing exclusivity or trademarks, or the risk of failure to obtain and enforce patent protection; the risk of substantial adverse litigation/government investigation claims and insufficient insurance coverage; effects of patent litigation in respect of IP rights; exchange rate fluctuations; the risk that R&D will not yield new products that achieve commercial success; the risk that strategic alliances and acquisitions, including licensing and collaborations, 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 delays 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 of outsourcing; the risks associated with manufacturing biologics; the risk of delay to new product launches; the difficulties of obtaining and maintaining regulatory approvals for products; the risk of failure to adhere to applicable laws, rules and regulations; the risk of failure to adhere to applicable laws, rules and regulations relating to anti-competitive behaviour; the risk that new products do not perform as we expect; failure to achieve strategic priorities or to meet targets or expectations; the risk of an adverse impact of a sustained economic downturn; political and socio-economic conditions; the risk of environmental liabilities; the risk of occupational health and safety liabilities; the risk associated with pensions liabilities; the risk of misuse of social medial platforms and new technology; the risks associated with developing our business in emerging markets; the risk of illegal trade in our products; the risks from pressures resulting from generic competition; the risk of failure to successfully implement planned cost reduction measures through productivity initiatives and restructuring programmes; economic, regulatory and political pressures to limit or reduce the cost of our products; 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; the impact of increasing implementation and enforcement of more stringent anti-bribery and anti-corruption legislation; and the risk of failure of information technology and cybercrime. Nothing in this presentation / webcast should be construed as a profit forecast.

Agenda

Unmet medical need	Dr Colin Reisner	
Results from the Phase III SIROCCO and CALIMA trials	Dr Mark FitzGerald	
Medical practice	Dr Andrew Menzies-Gow	
Looking forward	Tom Keith-Roach	

Key late-stage medicines & lifecycle

Phase III trials or under regulatory review*

Respiratory & Autoimmunity	Cardiovascular & Metabolic Diseases	Oncology	Infection, Neuroscience (opportunistic)
brodalumab* (psoriasis)	**ZS-9*** (hyperkalaemia)	**cediranib*** (ovarian cancer)	**AZD3293** (Alzheimer's disease)
benralizumab (severe asthma, COPD)	**roxadustat** (anaemia)	**selumetinib** (lung cancer)	
tralokinumab (severe asthma)	***Brilinta*** (heart disease)	**durvalumab** (multiple cancers)	
PT010 (COPD, asthma)		**durva + treme** (multiple cancers)	
anifrolumab (lupus)		**acalabrutinib** (blood cancers)	
		moxetumomab (leukaemia)	
		Lynparza (multiple cancers)	
		Tagrisso (lung cancer)	

Status as of 28 July 2016 (H1 2016 Results) New medicine with larger potential

Unmet medical need

AstraZeneca
What science can do

Dr Colin Reisner
Chief Medical Officer, Pearl Therapeutics and Head of Clinical, Respiratory Global Medicines, AstraZeneca

Asthma that is inadequately controlled by high-dose ICS-based therapy represents a significant healthcare burden

Asthma varies in disease severity[1,2,3]

315 million people
suffer from asthma worldwide

1 in 10 people (approx.)
with asthma have severe asthma, requiring:

High-dose ICS-based therapy + Other asthma medications

Linked to poor outcomes and medical emergencies[4,5]

In patients with uncontrolled asthma:

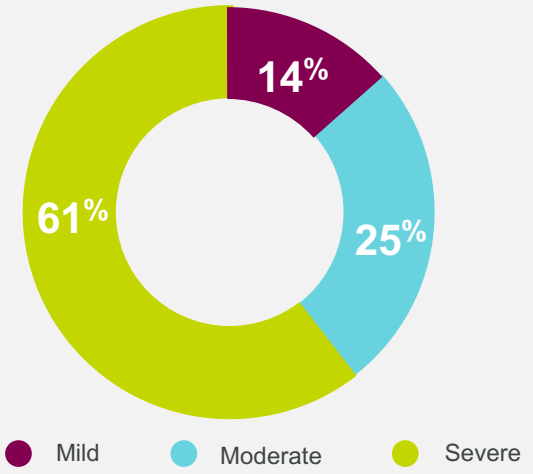
- **91%** have normal daily activities impacted at least once per week

In patients with uncontrolled severe asthma*:

- **8X** higher risk of death
- **10X** higher risk of hospital stays

Severe asthma accounts for majority of asthma costs[6]

Share (%) of total direct cost of asthma for different levels of severity



* Compares severe uncontrolled asthma with severe controlled asthma

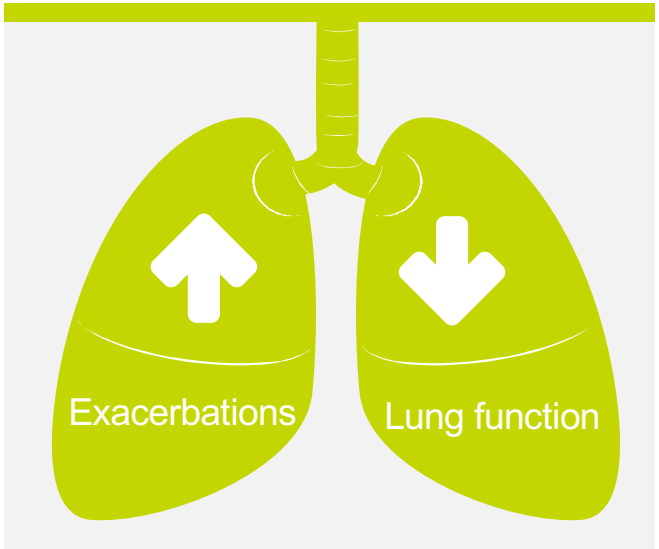
ICS, inhaled corticosteroids

1. Chung KF et al. Eur Respir J. 2014 Feb;43(2):343-73
2. To T et al. BioMed Central Public Health. 2012: 12(204)
3. Hekking PPW et al. J Allergy Clin Immun. 2015:135(4):896-902
4. Price D et al. NPJ Prim Care Respir Med 2014; 12; 24: 14009
5. Fernandes AG et al, J Bras Pneumol. 2014; 40(4): 364-372
6. Sadatsafavi M et al. Can Respir J 2010; 17: 74-80

Eosinophils are a therapeutic target in severe asthma

Persistent eosinophilia despite standard treatment is a recognized severe asthma phenotype

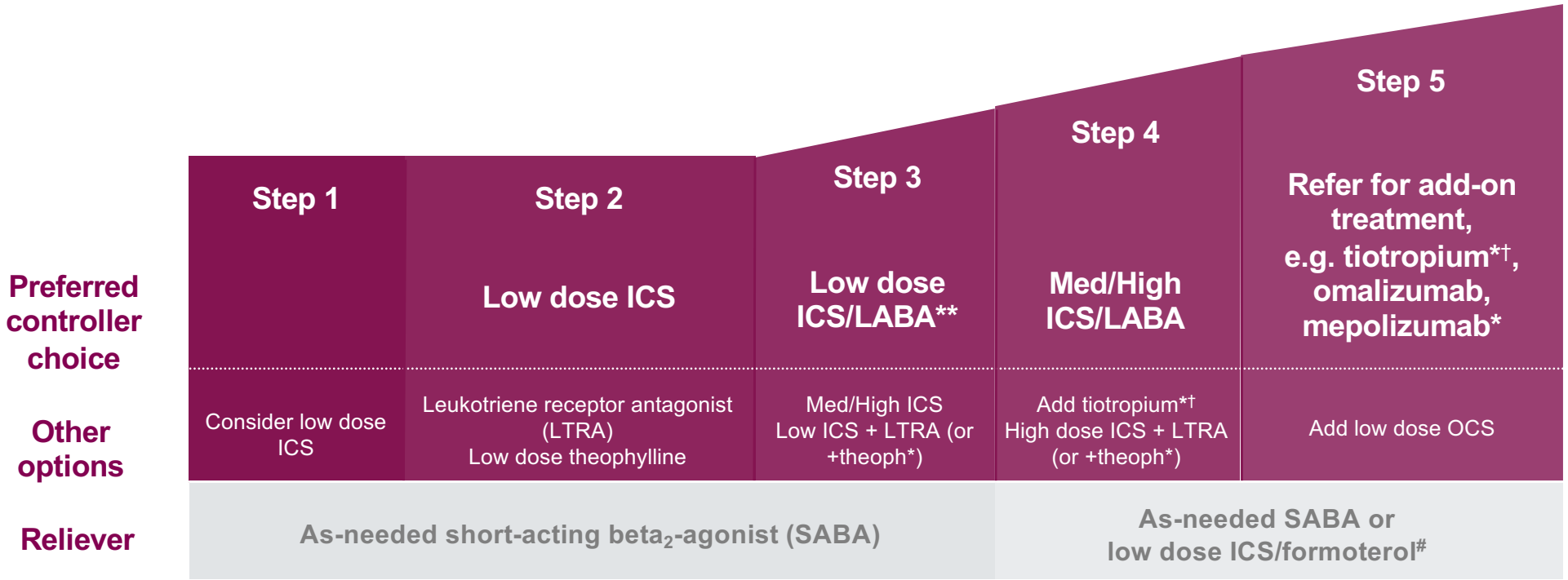
Eosinophilia is associated with increased risk of exacerbations and hospitalisations, and decreased lung function[1-5]



- Exacerbations are a constant risk for severe asthma patients despite current treatments; exacerbations are the regulatory standard for drug approval and highly relevant fro payers
- Patients are less able to breather normally (reduced FEV_1) leading to frequent symptoms and reduced quality of life

1. Garcia G et al. Eur Respir Rev. 2013;22(129):251-7
2. Green RH et al. Lancet. 2002;360(9347):1715-21
3. Di Franco A et al. J Asthma 2003; 40(2) 155-162
4. De Groot JC et al. ERJ Open Res 2015; 1: 00024
5. Hasegawa, K., and Jr. Camargo, C. A. Respirology 2016; 21: 761–764

GINA Guidelines



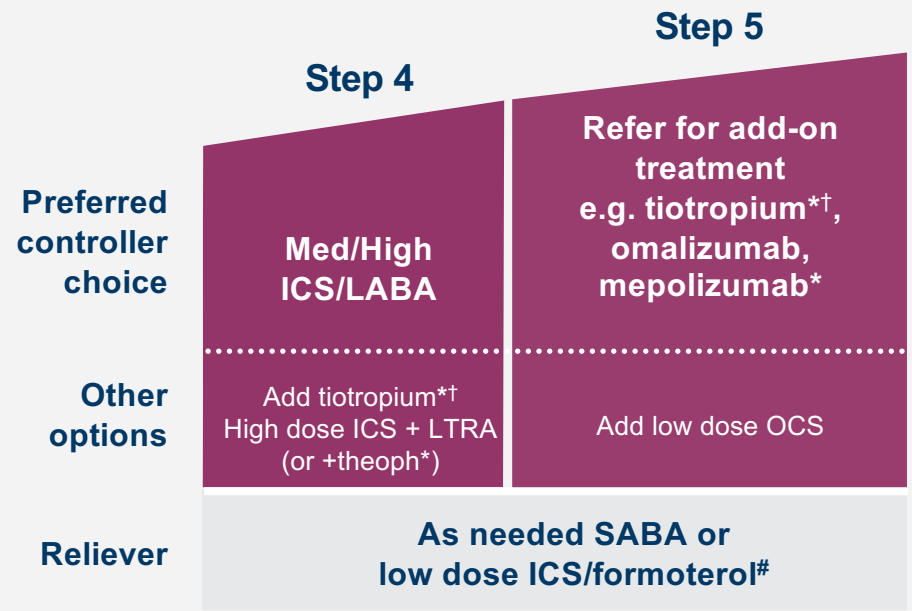
* Not for children <12 years.
** For children 6–11 years, the preferred Step 3 treatment is medium dose ICS.
# Low dose ICS/formoterol is the reliever medication for patients prescribed low dose budesonide/formoterol or low dose beclometasone/formoterol maintenance and reliever therapy.
† Tiotropium by mist inhaler is an add-on treatment for patients with a history of exacerbations; it is not indicated in children <12 years.

1. Global Initiative For Asthma (GINA). Global strategy for asthma management and prevention. Updated 2016. http://ginasthma.org accessed May 2016.
2. Adelphi. RESPIRATORY DSP® X-XII (2011-14). EU5 USA Japan and China Asthma COPD.

Step-care for asthma[1]

Approximately 40% of patients with severe asthma (step 4 or step 5 of GINA guidelines) remain uncontrolled on high-dose ICS + LABA[2]

GINA guidelines[1]:



IL-5 therapy currently available[3]:

	Mepolizumab	Reslizumab
Administration	100mg SC, Q4W (needs reconstituted)	3mg/kg IV infusion, Q4W
↓ exacerbations	✓	✓
↓ OCS use	✓	N/A
↑ lung function (FEV_1)	No consistent improvement	✓
Symptom (ACQ response[3])	SGRQ	ACQ

* Not for children <12 years.
# Low dose ICS/formoterol is the reliever medication for patients prescribed low dose budesonide/formoterol or low dose beclometasone/formoterol maintenance and reliever therapy
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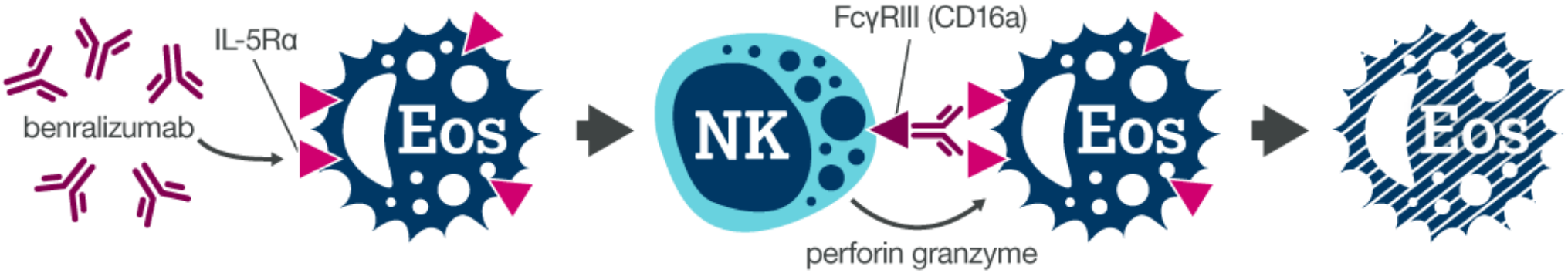
1. Global Initiative For Asthma (GINA). Global strategy for asthma management and prevention. Updated 2016. http://ginasthma.org accessed May 2016
2. Adelphi. RESPIRATORY DSP® X-XII (2011-14). EU5 USA Japan and China Asthma COPD
3. Pavord 2012; Ortega 2014 (MENSA); Castro 2015 (BREATH)
4. Saint George Respiratory Questionnaire; Asthma Control Questionnaire

Benralizumab (Anti-IL-5R α)

A targeted, anti-eosinophil therapy under investigation for asthma

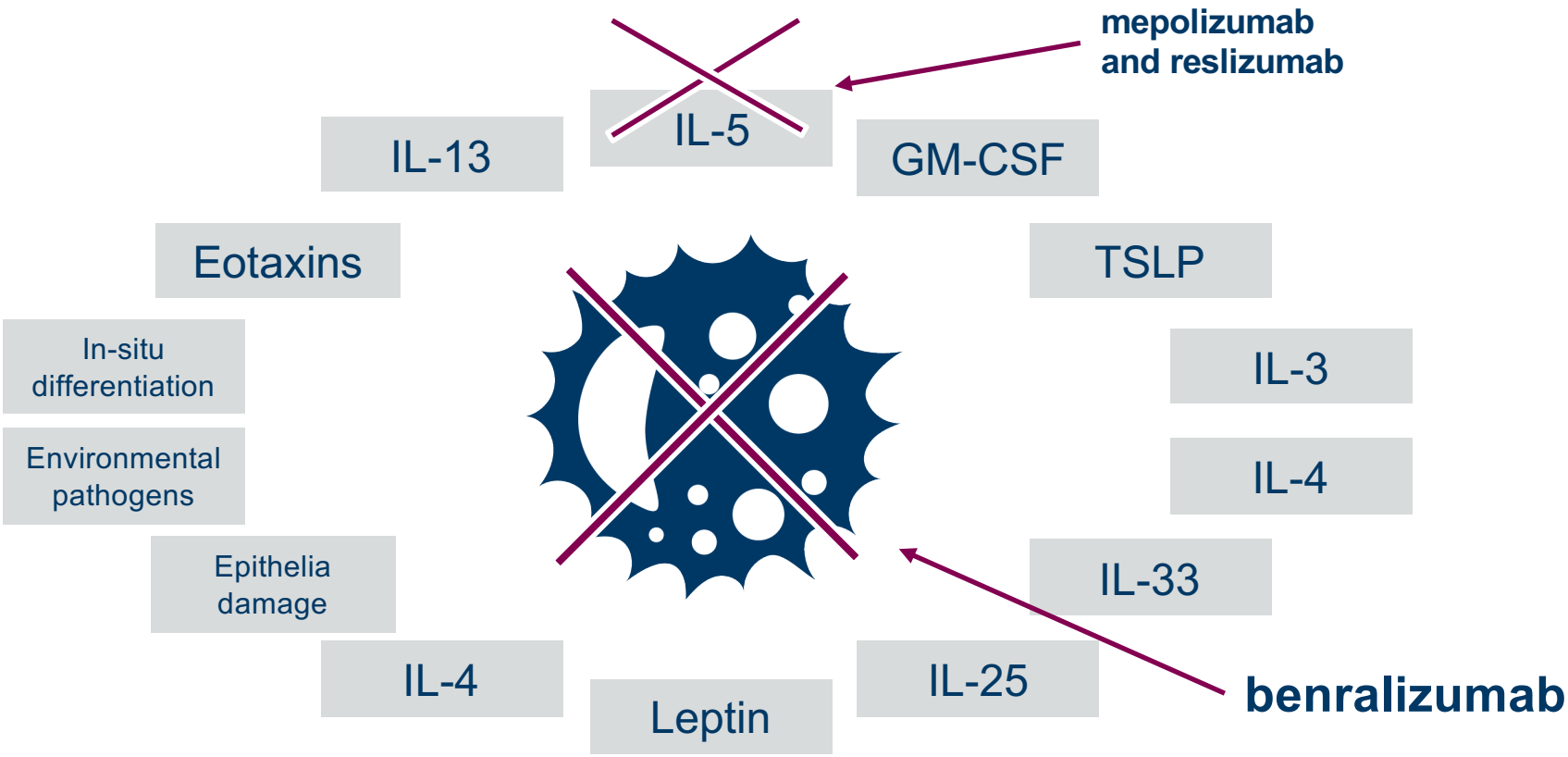
- Anti-eosinophil monoclonal antibody that depletes eosinophils via antibody-dependent cell-mediated cytotoxicity (ADCC), the process by which natural killer cells are activated to target eosinophils
- Induces direct, rapid, and near complete depletion of eosinophils in the bone marrow, blood and target tissue

Speed of peak effect in blood:	**Extent** of EOS reduction:	**Extent** of EOS reduction:
< 24 Hrs	**96% (lung)**	**100% (bone marrow)**



Only benralizumab directly targets the eosinophil

Anti-cytokine modalities have an indirect effect on eosinophil function



GM-CSF=granulocyte macrophage-colony stimulating factor; IL=interleukin; TSLP=thymic stromal lymphoprotein.

1. Shen Z, Malter JS. *Apoptosis*. 2015;20:224-234. 2. Mukherjee M et al. *World Allergy Organization Journal*. 2014;7:32.

WINDWARD

Phase III benralizumab clinical programme in asthma

- Largest known Phase III clinical trial programme of any respiratory biologic in asthma
- Comprises six Phase III trials in 3,068 patients and 798 sites, across 26 countries

SIROCCO[1] and CALIMA[2] - Efficacy and safety trials of benralizumab in patients with severe asthma

ZONDA[3] - Efficacy and safety trial of benralizumab to reduce oral corticosteroid use in patients with severe asthma on chronic OCS therapy

BISE[4] - Efficacy and safety of benralizumab in patients with mild to moderate asthma

GREGALE[5] - Functionality, reliability, and performance of the accessorised pre-filled syringe in an at-home setting

BORA[6] - Safety extension trial of patients coming from SIROCCO, CALIMA, and ZONDA

1. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/study/NCT01928771?term=NCT01928771&rank=1
2. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT01914757?term=calima&rank=1
3. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT02075255?term=zonda&rank=1
4. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT02322775?term=NCT02322775&rank=1
5. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT02417961?term=gregale&rank=1
6. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT02258542?term=bora&rank=2

Results from the Phase III SIROCCO and CALIMA trials in severe asthma

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Dr Mark FitzGerald
Director, Centre for Heart and Lung Health, Vancouver Coastal Health Research Institute, University of British Columbia, Canada

Institute for
HEART+LUNG Health
Strong beats. Clear breaths. Full lives.

Results from the Phase III SIROCCO and CALIMA trials in severe asthma

J Mark FitzGerald
Severe Asthma Clinic, VGH
University of British Columbia

Conflicts of Interest

- Research funding and/or honoraria from AstraZeneca, Boehringer-Ingelheim, Genentech, GlaxoSmithKline, Hoffmann-La Roche, MedImmune, Merck, Novartis
- BC Ministry of Health
- Member GINA Executive and of GINA Science Committee

Common study objectives: To evaluate the safety and efficacy of benralizumab 30mg sc Q4W or Q8W in severe asthma

PRIMARY ENDPOINT	• Annual rate of asthma exacerbations
KEY SECONDARY ENDPOINTS	• FEV_1 • Total asthma symptom score
OTHER SECONDARY ENDPOINTS	• ACQ-6 score • AQLQ(S)+12 score

The primary analysis population was patients receiving high-dosage ICS/LABA with blood eosinophils ≥300 cells/µL at baseline

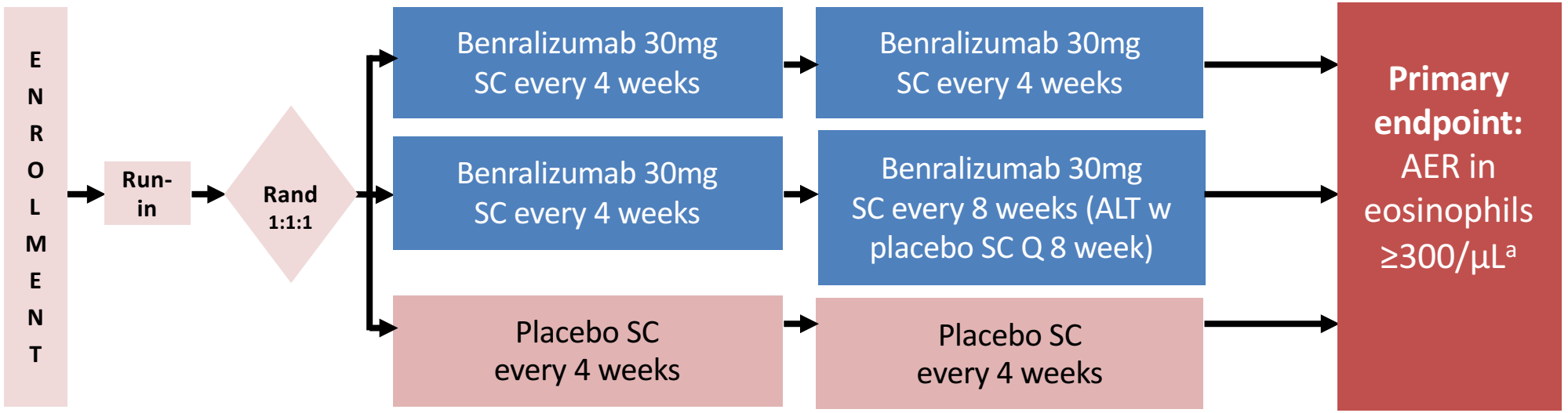
Only primary and key secondary endpoints are multiplicity protected; all other p values are nominal

Key inclusion criteria

- Males and females, aged 12–75 years
- Physician-diag. asthma requiring high-dosage ICS/LABA
  - Medium dose ICS/LABA cohort included in CALIMA
- ≥2 asthma exacerbations in the previous 12 months
- Symptomatic during run-in

SIROCCO (48 WK), CALIMA (56 WK): Common design

Planned 2:1 randomization ratio by eos (≥300/µL vs <300/µL)



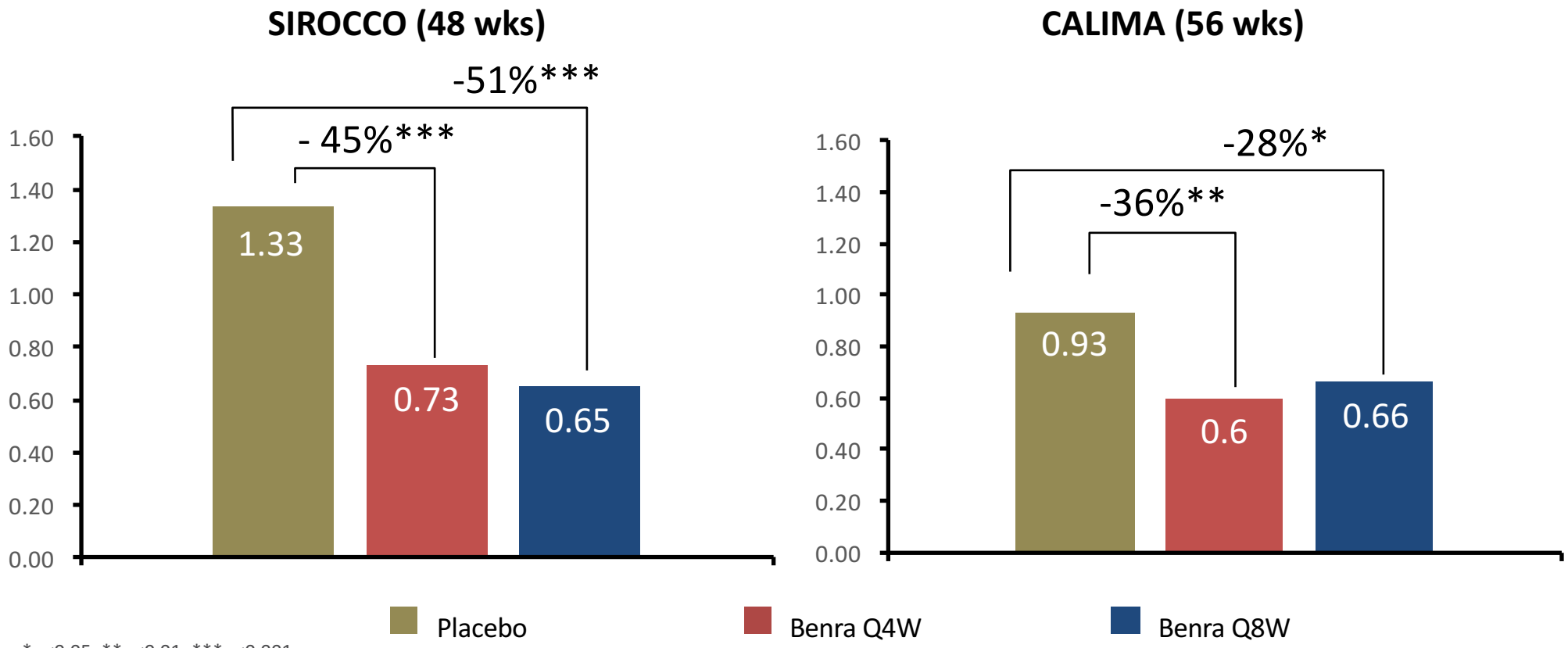
Visit 1	V2, V3; Run-in from V2–V4	V4 (week 0)	V4–V7 (weeks 0–8) V8–V16 (weeks 12–44) V17 (week 48)	FU V18 (week 56)	**SIROCCO**
			V4–V7 (weeks 0–8) V8–V18 (weeks 12–52) V19 (week 56)	FU V20 (week 60)	**CALIMA**

Baseline disease state characteristics were consistent with an uncontrolled asthma population (full analysis set)

	SIROCCO			CALIMA[a]		
	Benra Q4W N=399	Benra Q8W N=398	Placebo N=407	Benra Q4W N=425	Benra Q8W N=441	Placebo N=440
Gender: female, n (%)	275 (68.9)	252 (63.3)	269 (66.1)	270 (63.5)	273 (61.9)	264 (60.0)
Age (years), mean (SD)	50.1 (13.4)	47.6 (14.5)	48.7 (14.9)	50.0 (13.6)	49.0 (14.3)	48.8 (15.1)
Pre-BD FEV_1 (% PN), mean (SD)	57.4 (14.1)	56.1 (14.6)	56.6 (15.0)	58.9 (14.8)	57.9 (14.9)	58.0 (14.9)
ACQ-6 score, mean (SD)	2.8 (1.0)	2.8 (0.9)	2.9 (0.9)	2.7 (0.9)	2.8 (0.9)	2.7 (0.9)
Age (years) at diagnosis, median	35.1	31.4	31.5	32.7	30.9	29.5
Prior year exacerbations, mean (SD)	2.9 (1.8)	2.8 (1.5)	3.0 (1.8)	2.7 (1.9)	2.7 (1.42)	2.7 (1.63)
Atopic (phadiatop test), n (%)	231 (57.9)	244 (61.3)	230 (56.5)	264 (62.1)	278 (63.0)	286 (65.0)
Local eos (cells/µL), mean (SD)	491 (413.8)	470 (392.8)	457 (366.3)	462 (349.3)	465 (359.6)	488 (444.8)
Local eos ≥ 300 subgroup	638 (417.4)	620 (397.6)	621 (351.4)	607 (339.1)	623 (346.5)	639 (469.2)

[a]High and medium dose ICS combined.
ACQ-6=asthma control questionnaire 6; BD=bronchodilator; eos=baseline blood eosinophil count; FEV_1=forced expiratory volume in one second; PN=predicted normal; SD=standard deviation.

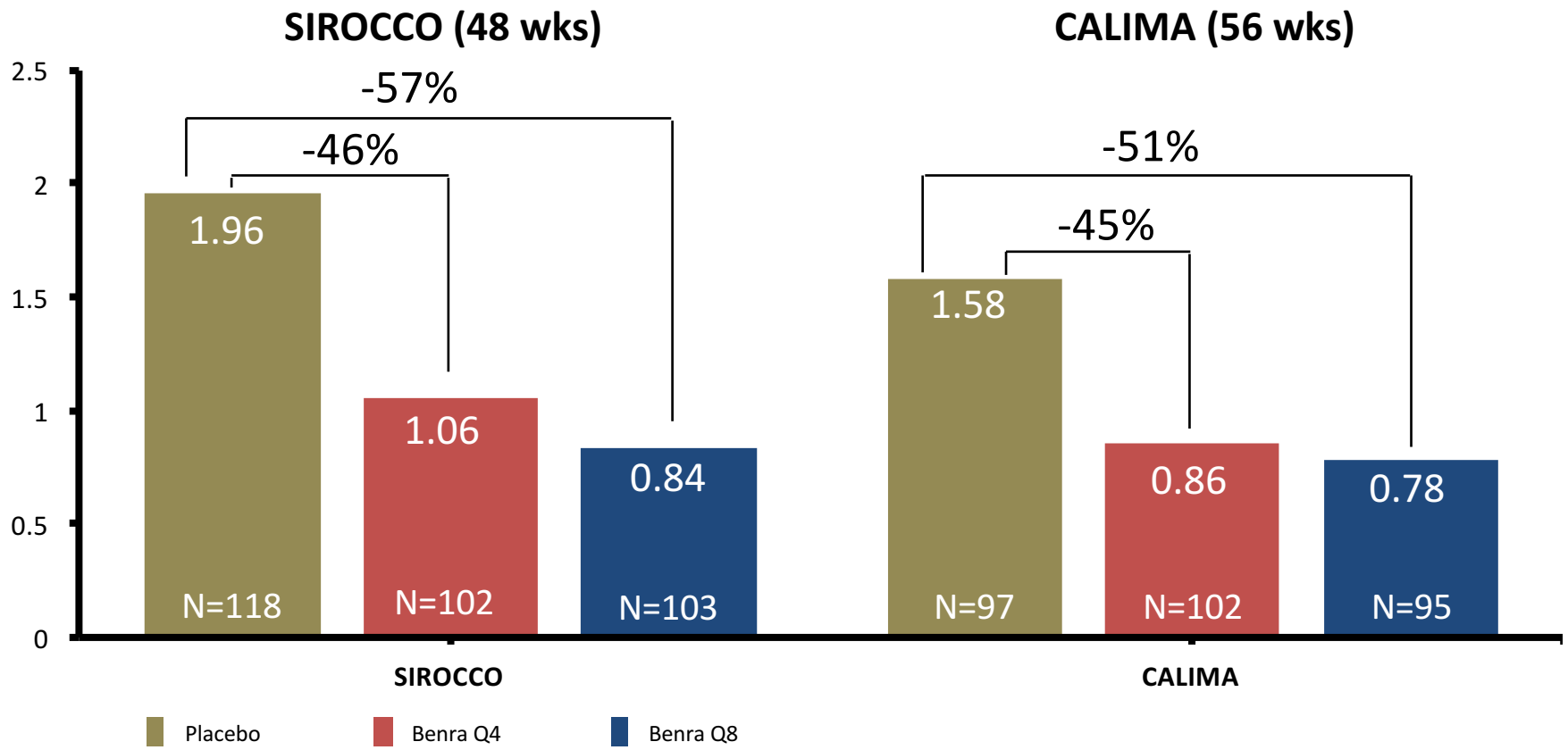
Benralizumab significantly reduced annual asthma exacerbation rate, AER



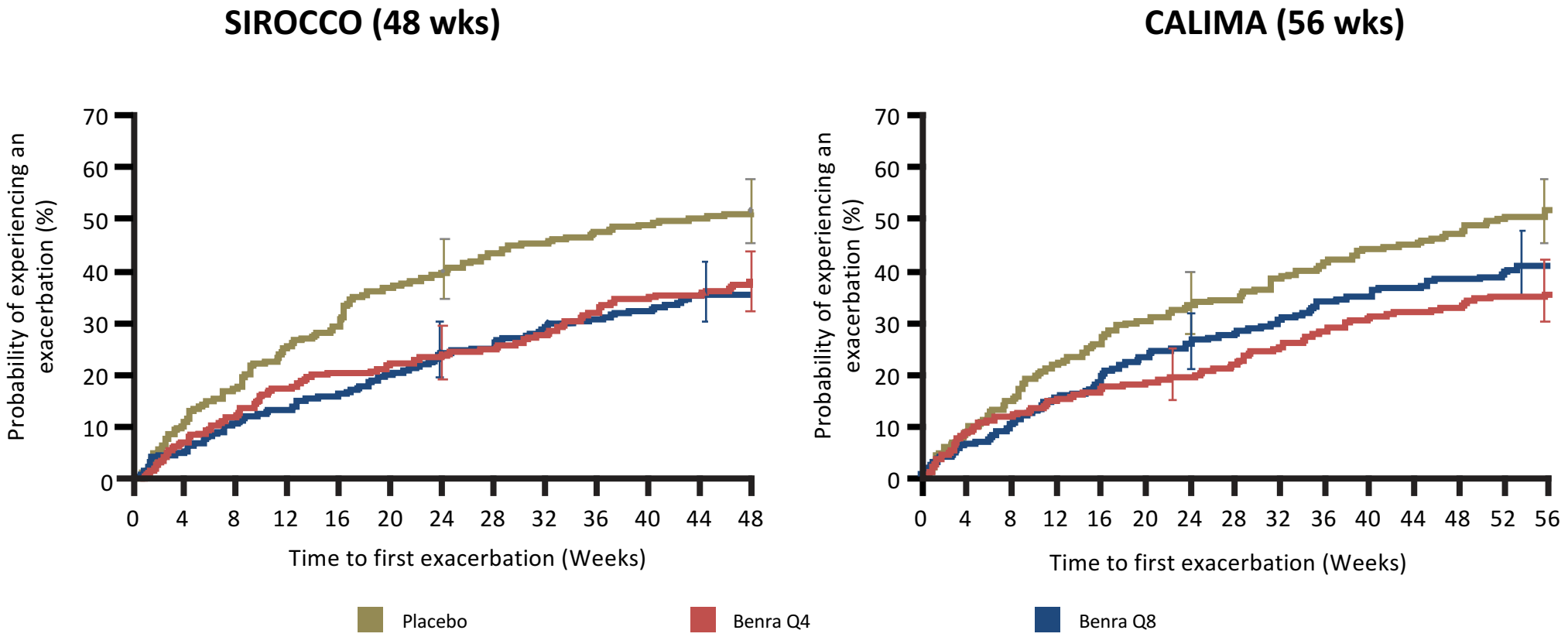
*p<0.05; **p<0.01; ***p<0.001
eos, baseline blood eosinophil count; ICS, inhaled corticosteroid

SIROCCO and CALIMA: patients with ≥3 prior exacerbations

Benralizumab produced a similar magnitude of exacerbation reduction in higher risk patients

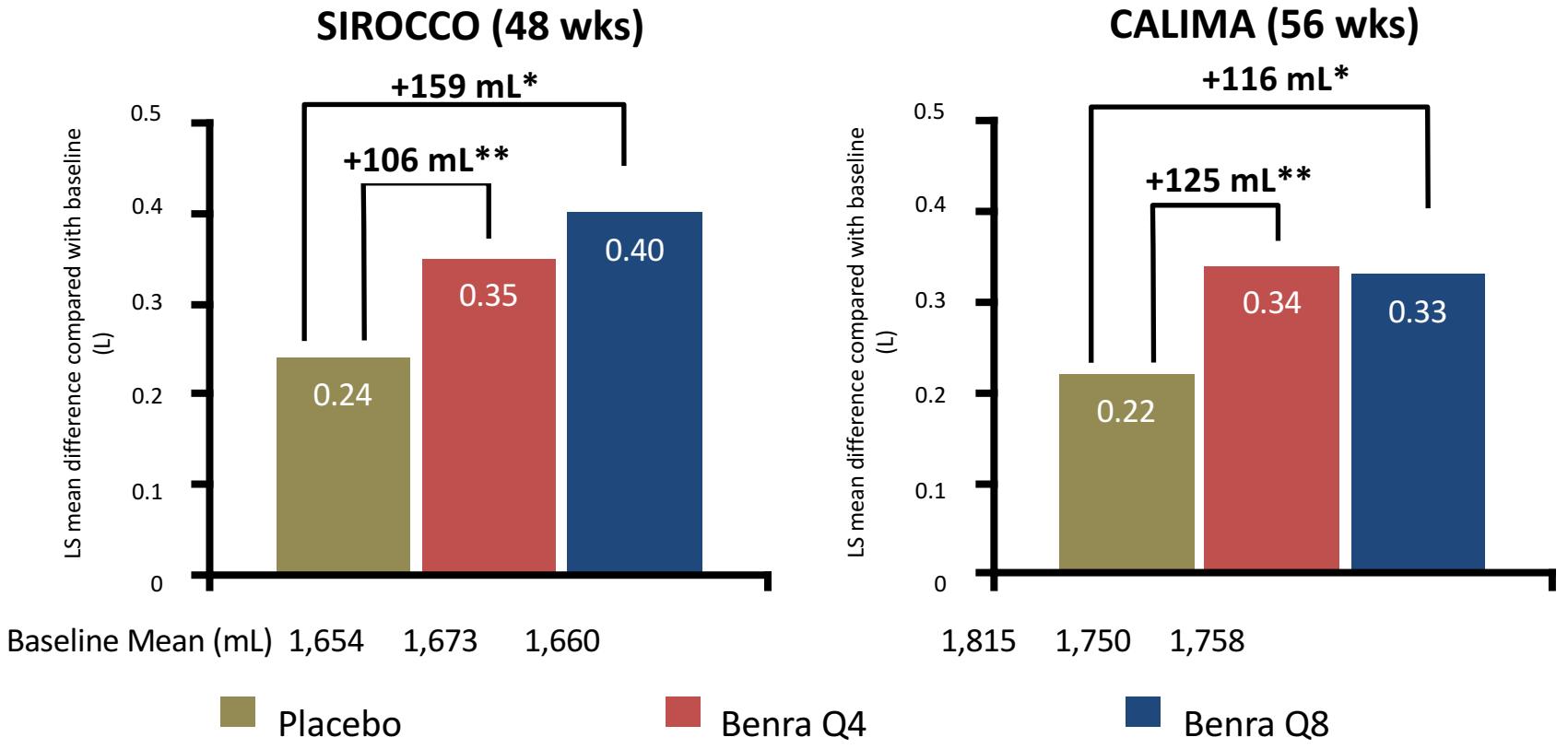


Prolonged time to first exacerbation



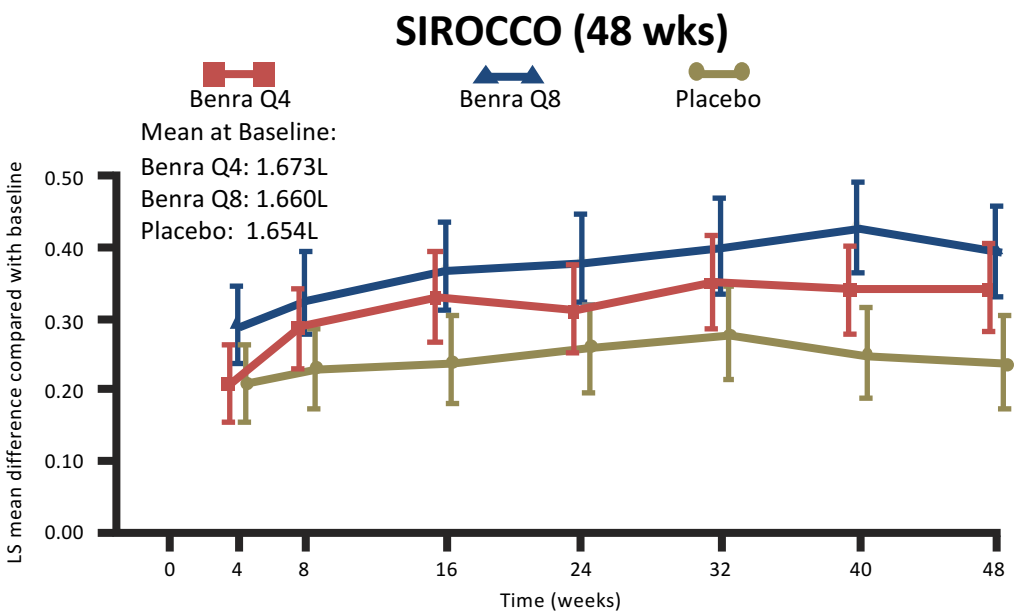
ICS, inhaled corticosteroid

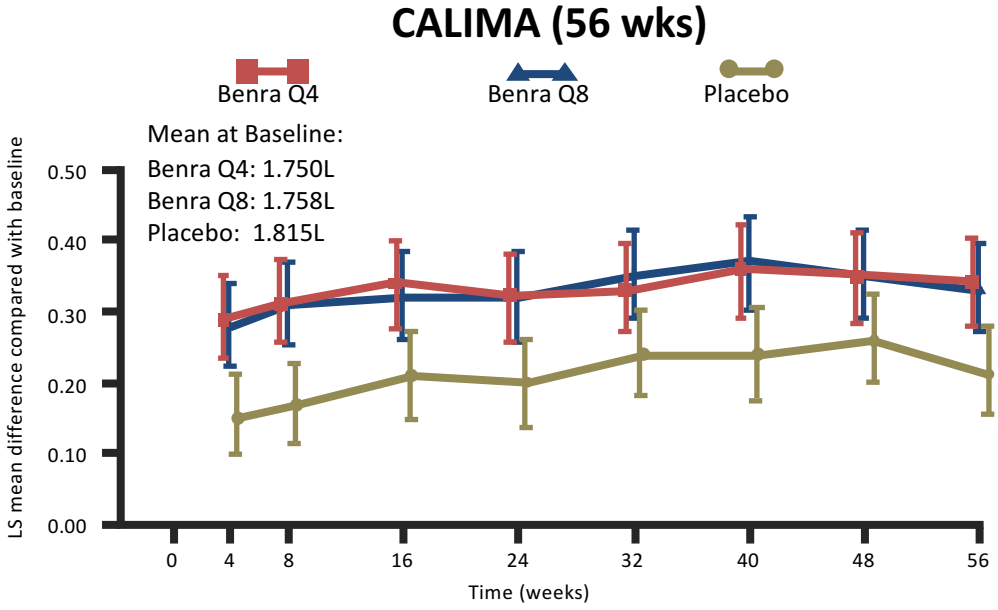
Benralizumab significantly improved lung function (FEV_1†)



*p<0.05; **p<0.01; †Analysis via Negative binomial adjusting for treatment, region, exacerbations in previous year, OCS (Yes/No)
eos, baseline blood eosinophil count; FEV_1, forced expiratory volume in one second; ICS, inhaled corticosteroid; LS, least squares; OCS, oral corticosteroid

Improvement in FEV_1 seen after the first dose of benralizumab; maintained throughout the treatment period



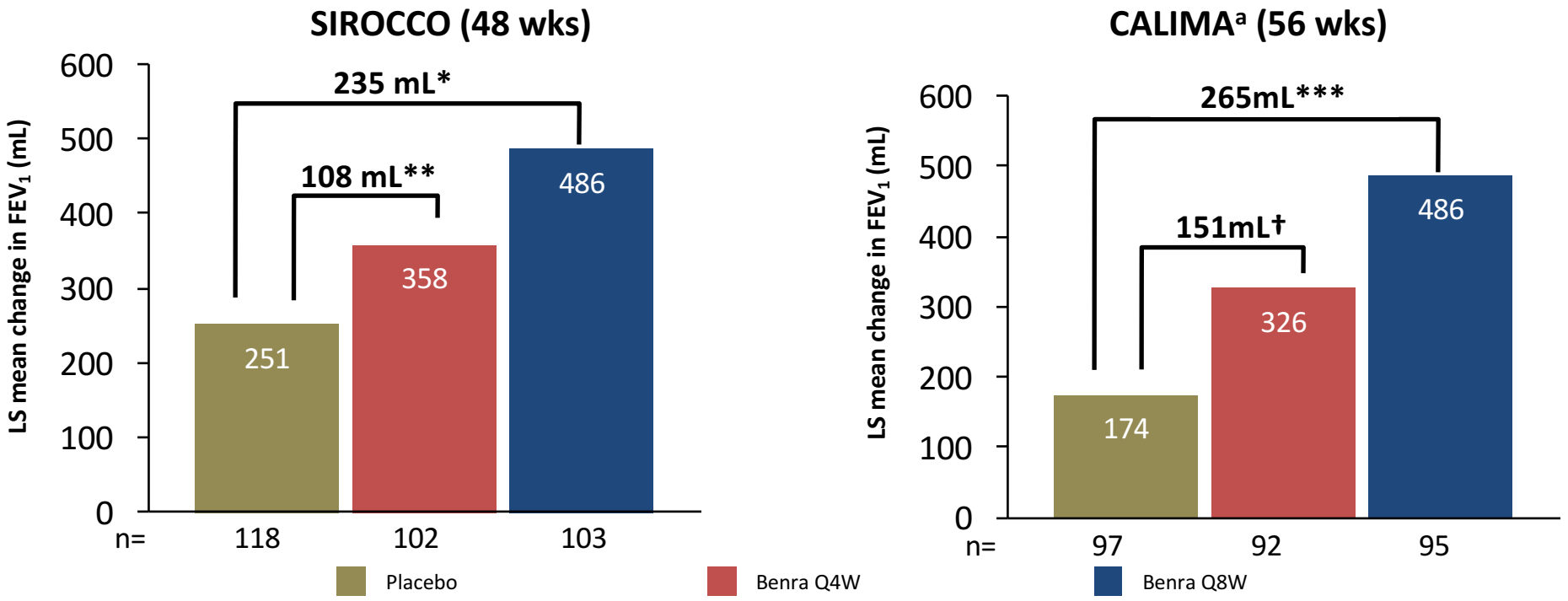


56/48 wks	Group LS MEANS	LS MEAN Difference (95% CI)	Group LS MEANS	LS MEAN Difference (95% CI)
Q4 – Placebo	0.345 vs 0.239	0.106 (0.016, 0.198); p=0.022	0.340 vs 0.215	0.125 (0.037, 0.213); p=0.005
Q8 - placebo	0.398 vs 0.239	0.159 (0.068, 0.249); p=0.001	0.330 vs 0.215	0.116 (0.028, 0.204); p=0.010

*p<0.05 Benra Q4 vs placebo; +p<0.05 Benra Q8 vs placebo; error bars represent 95% CIs; analysis via mixed effect model repeat measurement (baseline, oral corticosteroid use, region, treatment, treatment duration)
CI, confidence interval; FEV1, forced expiratory volume in one second; LS, least squares

SIROCCO and CALIMA: patients with ≥3 prior exacerbations

Benralizumab produced a greater magnitude of lung function improvement in higher risk patients

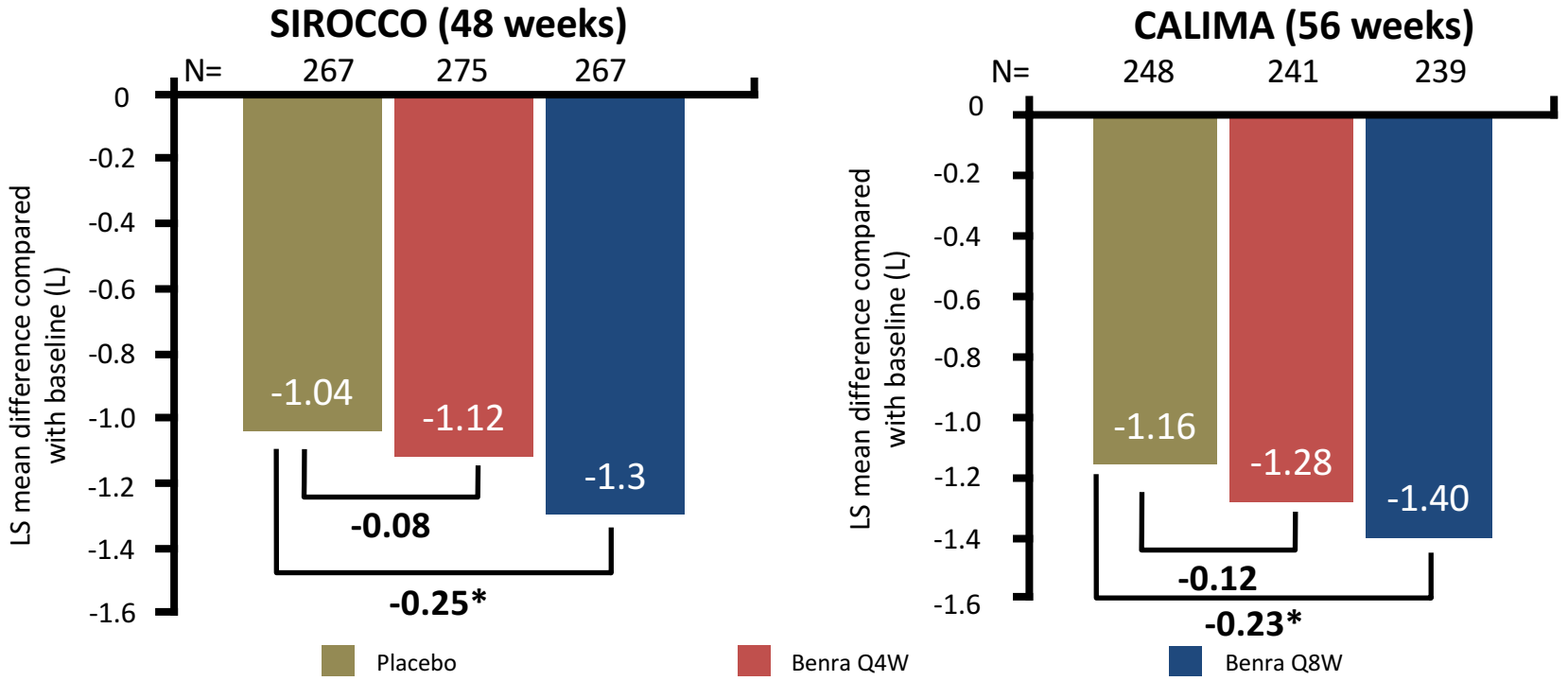


[a] Data for CALIMA from high-dosage ICS cohort

*P=0.0018; **P=0.1510; ***P= 0.0006; † P=0.0481

benra=benralizumab; eos=baseline blood eosinophil count; FEV_1=forced expiratory volume in 1 second; LS=least squares; Q4W=every 4 weeks; Q8W=every 8 weeks.

Benralizumab Q8W significantly improved total daily asthma symptom score compared to placebo



Patient reported measures of control (ACQ6 score) and quality of life (AQLQ score) also improved with benralizumab Q8W in both trials, with responder analyses favoring treatment

*P<0.05.

Analysis via mixed effect model repeat measurement adjusting for treatment, region, baseline, OCS (Yes/No).

eos=baseline blood eosinophil count; ICS=inhaled corticosteroid; LS=least squares; Q4W=every 4 weeks; Q8W=every 8 weeks.

The overall and serious adverse event (AE) frequencies in both studies were similar for benralizumab and placebo in each study

- The most common AEs (≥ 5%) were consistent with an uncontrolled asthma population
- Imbalance in the frequency of DAEs: mostly single events with no trend in types of events
- ADA response detected in 10-15%: no apparent impact on efficacy or safety

	SIROCCO (48 Weeks)			CALIMA(56 Weeks)		
	Benra Q4 n=403	Benra Q8 n=394	Placebo n=407	Benra Q4 n=438	Benra Q8 n=428	Placebo n=440
Any Adverse Event	293 (72.7)	281 (71.3)	311 (76.4)	322 (73.5)	320 (74.8)	342 (77.7)
Any Serious Adverse Events (SAE)	47 (11.7)	52 (13.2)	55 (13.5)	45 (10.3)	40 (9.3)	60 (13.6)
Any Discontinuation Adverse Event (DAE)	9 (2.2)	8 (2.0)	3 (0.7)	8 (1.8)	10 (2.3)	4 (0.9)
Injection site reactions	16 (4.0)	9 (2.3)	8 (2.0)	11 (2.5)	9 (2.1)	8 (1.8)
Hypersensitivity AEs	13 (3.2)	11 (2.8)	11 (2.7)	13 (3.0)	15 (3.5)	18 (4.1)
Any AE outcome = death*	2 (0.5)	1 (0.3)	2 (0.5)	2 (0.5)	2 (0.5)	-

*No death was assessed as treatment-related

AE, adverse event; DAE, drug-related AE; SAE, serious AE; ADA, anti-drug anti-body; IP, investigational product

Conclusions: Benralizumab 30mg sc significantly improved multiple measures of asthma control in two Phase 3 trials

- In patients with severe eosinophilic asthma uncontrolled on standard-of-care ICS/LABA treatment, benralizumab:
  - Reduced annual asthma exacerbation rates (up to 51%)
  - Improved lung function (up to 159 mL in FEV_1): improvements observed after first dose and sustained throughout treatment
  - Improved daily asthma symptoms, such as wheeze, cough and shortness of breath
  - Improved patient reported measures of asthma control and quality of life
- Efficacy results achieved for Q8W dosing were similar or numerically larger than for Q4W dosing regimen
- Frequency and nature of adverse events similar to placebo
- Benralizumab unique anti-eosinophil mechanism of action represents a new option for the treatment of severe eosinophilic asthma

Medical practice

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Dr Andrew Menzies-Gow
Consultant in Respiratory Medicine, and Director, Lung Division, Royal Brompton Hospital, London

How do you define a patient with ‘severe asthma’? How are they treated with todays’ standard of care? What are the greatest remaining unmet needs?

How important is exacerbation history? What is the relationship between eosinophil levels and asthma severity?

How does benralizumab compare versus current therapies? What's your view?

What will it take for biologics to be a greater part of asthma care? How do healthcare systems need to evolve?

Looking forward

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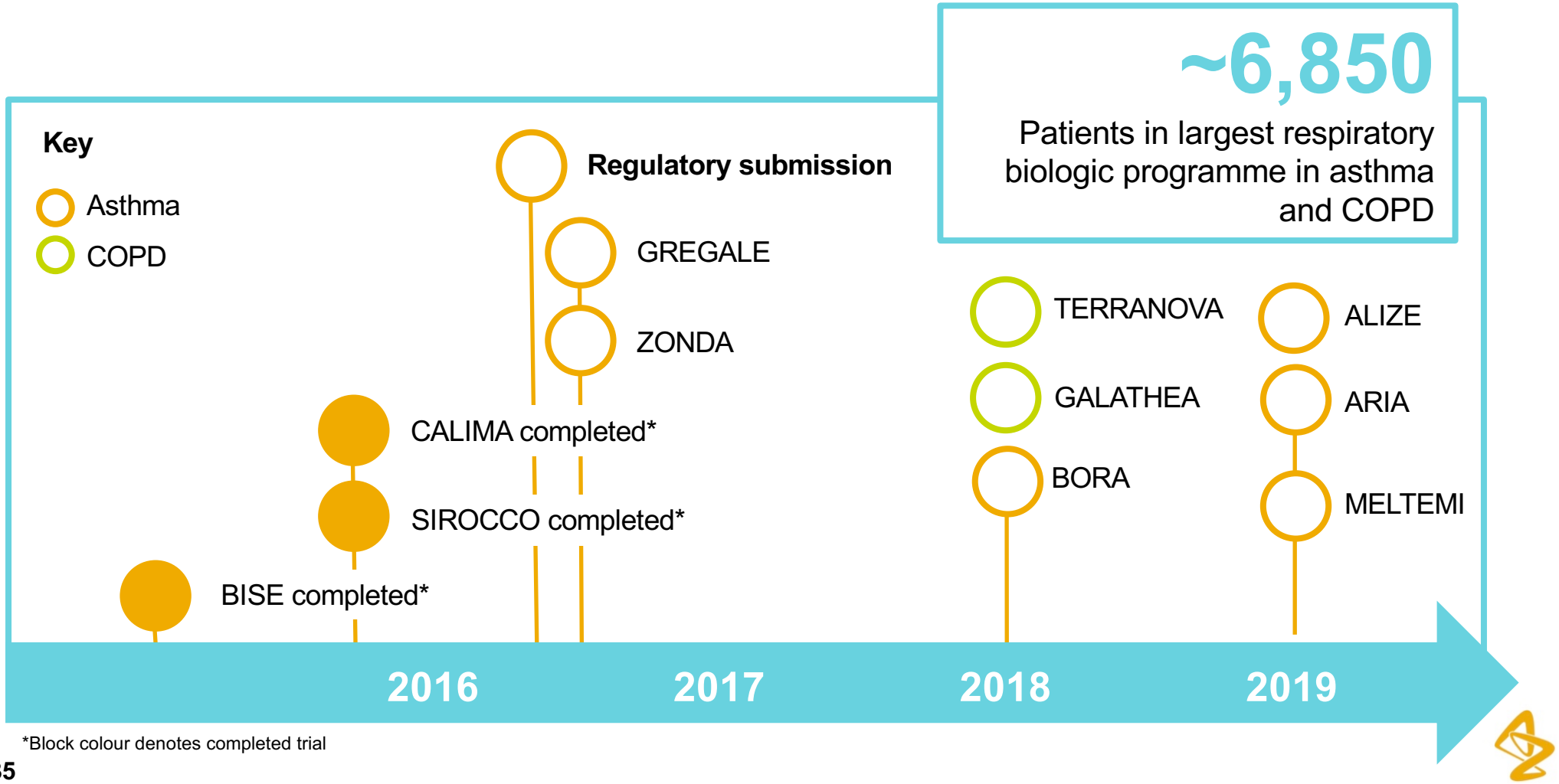
Tom Keith-Roach
Head of Global Product & Portfolio Strategy, Respiratory, AstraZeneca

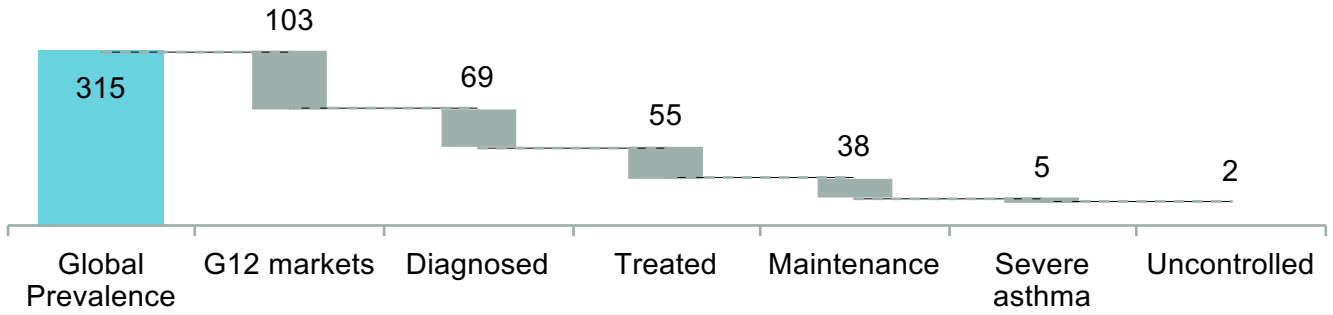
Benralizumab regulatory submission expected in H2 2016



*Block colour denotes completed trial

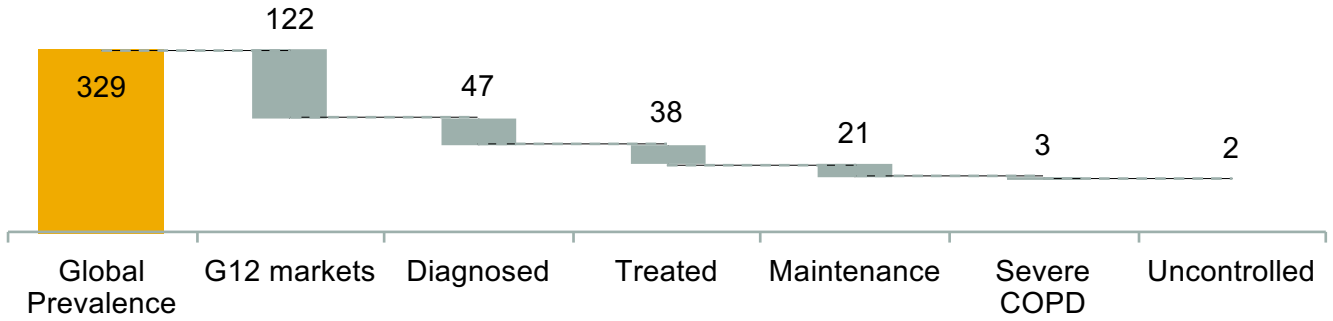
High economic burden and a clear unmet need will continue to drive the severe asthma and COPD market

Asthma, 2015, G12 Markets[1, 2]



Asthma, rates[1]	2015	2025
Prevalence	315	↑
Diagnosis	68%	↑
Treatment	77%	↑
Biologic	9%	↑

COPD, 2015, G12 Markets[1, 2]



COPD, rates[1]	2015	2025
Prevalence	345	↑
Diagnosis	39%	↑
Treatment	80%	↑
Biologic	0%	↑

1. AstraZeneca analysis supported by Decision Resources, IMS MIDAS and IMS longitudinal data and other specific country sources
2., Markets include: US, EU5 (United Kingdom, Germany, Italy, France, Spain), Japan, China, Canada, Australia, Brazil and Russia

Summary

1	2	3
Positive Phase III data with SIROCCO and CALIMA	**Execution priorities**	**Future milestones**
Efficacy across exacerbations, lung function and symptoms	US and EU regulatory submissions H2 2016	ZONDA presentation H1 2017
Lung function improvements at 4-weeks; sustained at 52-weeks	Full launch preparation underway	VOYAGER data (COPD) 2018
Convenient dosing		

Q&A

AstraZeneca
What science can do

Investor science conference call
European Respiratory Society

07 September 2016