

Break-out session 4

Respiratory & Immunology: near- term opportunities

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Interactive event for investors and analysts. This webinar is being recorded.
https://astrazeneca.zoom.us/webinar/register/WN_WkP2l8waRWiC0a9ROqIkUQ



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Respiratory diseases

Under recognised and under treated



Asthma

339m
patients
worldwide

176m
attacks
each year

>50%
remain
uncontrolled

~34m
with severe
disease

50%
of asthma healthcare
costs from severe disease



COPD¹

384m
patients worldwide

3rd
cause of death in 2020, more
deaths than cancer each year

20%
will die within one year
after 1st hospitalisation

One
COPD exacerbation can more than
double the rate of lung function decline



Evidence to transform care



- ICS²/formoterol preferred anti-inflammatory reliever in asthma [Symbicort]
- Biologics standard of care for severe asthma and to reduce need for OCS³ [Fasenra]
- Beneficial effects on mortality from triple therapy in COPD [Breztri]

Sources: GINA, The Global Asthma Report 2018. AZ ID:SD-3010-ALL-0017. Davis J, Trudo F, Siddall J, et al. *Journal of Asthma*, 2019; 56:3, 332-340. Wenzel S. *Am J Respir Crit Care Med*. 2005;172:149-160. WAO, The management of severe asthma: economic analysis of the cost of treatments for severe asthma [online].

Sources: Adeniyi D, et al. *J Glob Health*. 2015;5(2):020415. WHO, The top 10 causes of death [online]. GOLD, 2020 report. Ho-TW, et al. *PLoS ONE*. 2014;9(12):e114866. Halpin DMG et al, *Respir Med* 2017;128:85-91
1. Chronic obstructive pulmonary disease.

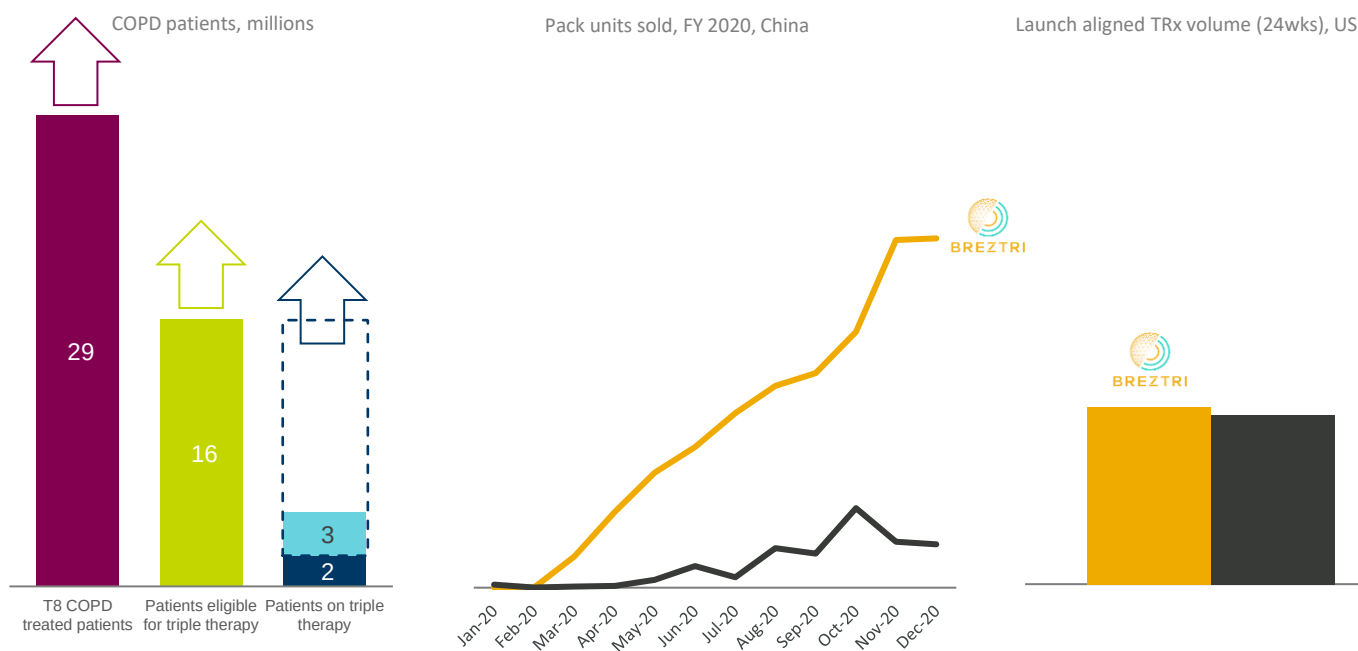
Source: Martinez FJ, et al. *Am J Resp and Crit Care Med*. 2020;201: A4214.
2. Inhaled corticosteroids 3. Oral corticosteroids.



Breztri and PT027: strength in inhaled medicines

Next-generation medicines for mild and moderate disease

Breztri: poised to be a strong competitor in the fastest-growing COPD class



Encouraging performance seen in China and US
Asthma programme in progress, data readout 2022+

Fixed triple Open triple Breztri Competitor

Source: IQVIA China hospital sales Jan-Dec 2020; IQVIA weekly data - week ending 12/03/21, Breztri week one = week ending 02/10/20, Competitor week one = week ending 03/11/17. T8 markets are US, EU5, China and Japan.

PT027: first ICS/SABA¹ rescue medicine for the US

- Replace traditional SABA rescue approach with 'as needed' ICS/SABA to treat underlying inflammation
- Phase III results in H2 2021

"Concomitant ICS and SABA taken as needed is a preferred option at Step 2"

2020 US National Asthma Education and Prevention Program guidelines

71m

rescue inhalers used in the US per year



Rescue medicines valued at \$2.5bn

Sources: NIH, NAEPP report: 2020 focused updates to the asthma management guidelines [online]. IQVIA, MAT sales 2020, Rescue defined as SABA only.

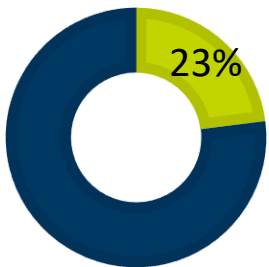
1. Short-acting beta agonist.



Fasenra and tezepelumab: asthma leadership

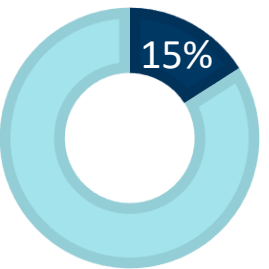
Greater use of biologics anticipated in severe asthma

Significant opportunity to grow biopenetration in severe asthma



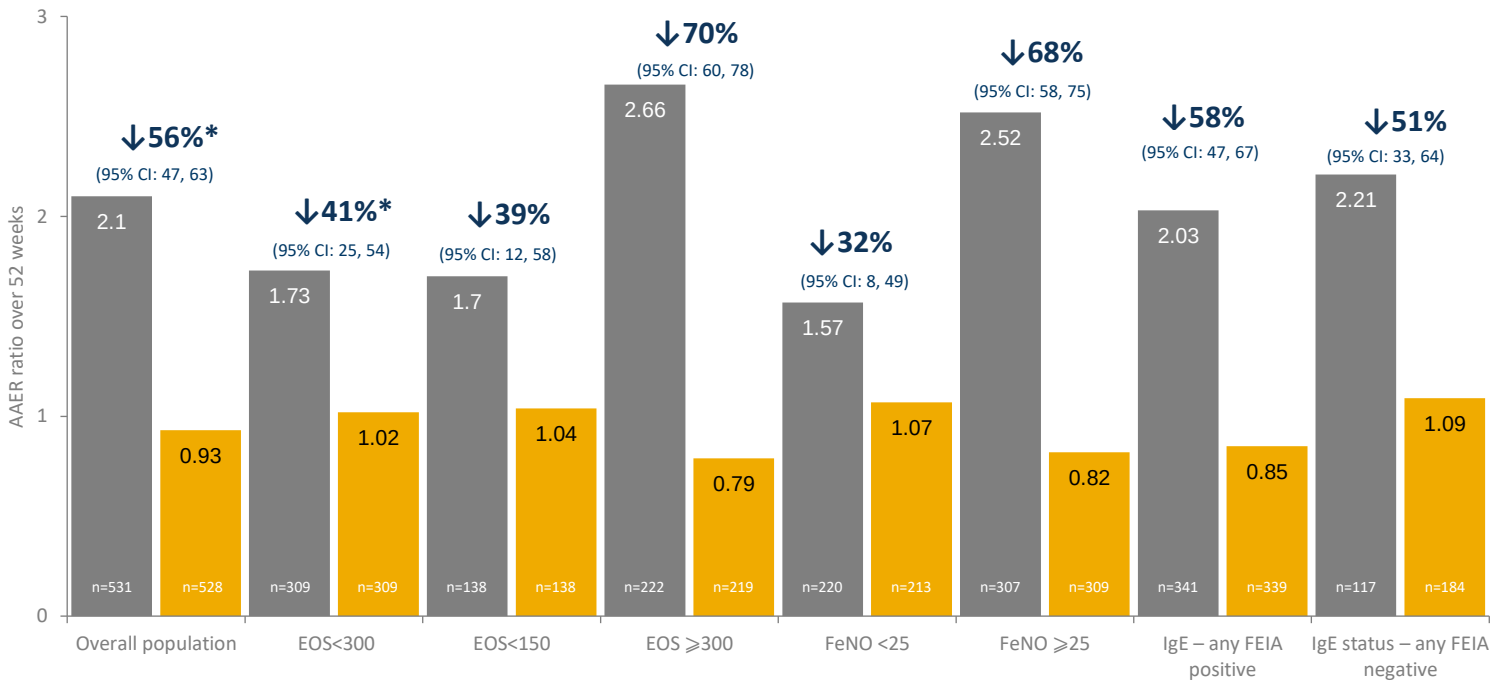
Fasenra remains key choice for high EOS¹ patients

TRx² 23% | NBRx³ 28%
New PONENTE data in OCS



Only 15% of eligible patients have access to a biologic (RA⁴ ~45% in US)

Tezepelumab⁵: positive NAVIGATOR Phase III data in broad population



The first and only biologic to demonstrate AAER⁶ reduction irrespective of baseline blood EOS, FeNO⁷, and allergic status

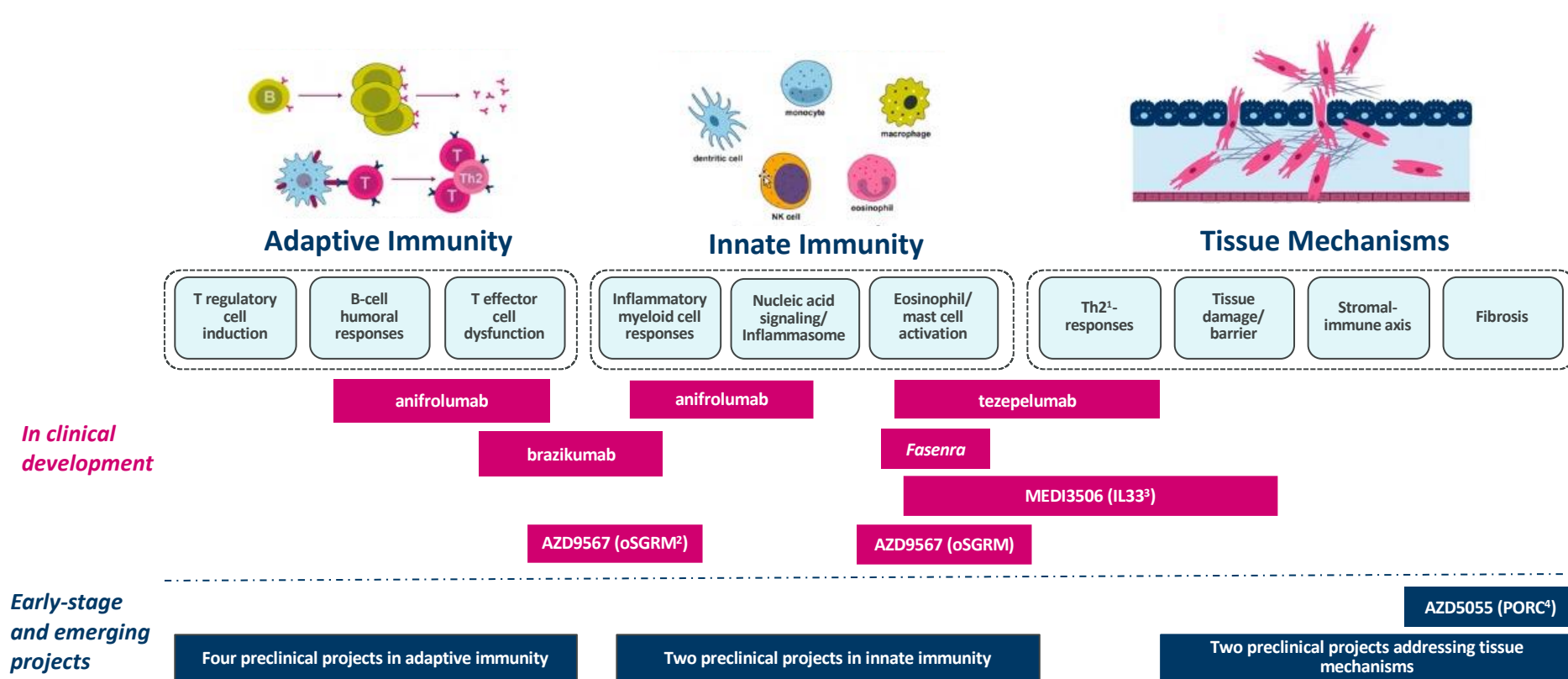
Sources: Menzies-Gow A, et al. Poster presented at the AAAAI Annual Meeting, 26 February to 1 March 2021. L45. Source: Latest market share from IQVIA, T7 markets: US, EU5, Japan. 1. Eosinophilic 2. Total prescriptions, exit share Dec 2020 3. New-to-brand prescriptions, YTD Dec 2020 4. Rheumatoid arthritis.

tezepelumab placebo Sources: Menzies-Gow A, et al. Poster presented at the AAAAI Annual Meeting, 26 February to 1 March 2021. Hanania NA, et al. *Ann Intern Med*. 2011;154 (9):573-82. Yancey SW, et al. *Respir Med* 2019;151:139-141. FitzGerald JM, et al. *Lancet Respir Med* 2018;6(1):51-64. Castro M, et al. *N Engl J Med*. 2018;378(26):2486-2496. Ortega HG, et al. *N Engl J M* 2014;371(13):1198-207. Wenzel S, et al. *Lancet* 2016;388(10039):31-44 5. In collaboration with Amgen Inc. 6. Annualised asthma exacerbation rate 7. Fractional exhaled nitric oxide.



Increasing presence in immunology

Pursuing leadership, starting with lupus



Near term

- Enter rheumatology with anifrolumab in systemic lupus erythematosus

Medium term

- Expand anifrolumab in interferon diseases
- Launch *Fasenra* and tezepelumab LCM⁵ indications
- Enter Crohn's disease and ulcerative colitis with brazikumab

Long term

- Novel pathways with disruptive potential

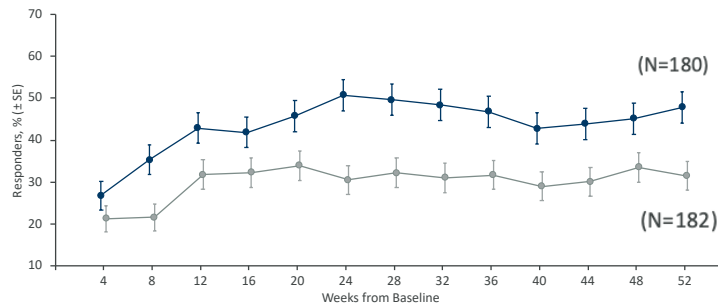
1. T helper type 2 2. Oral selective glucocorticoid receptor modulator 3. Interleukin 33 4. Porcupine inhibitor 5. Life cycle management. Source: AstraZeneca data on file.



Anifrolumab: first new SLE¹ treatment in 10 years

Potential first-in-class MOA² with robust efficacy. LCM plans include LN³, CLE⁴, myositis

TULIP 2 Phase III trial BICLA⁵ scores, overall responders

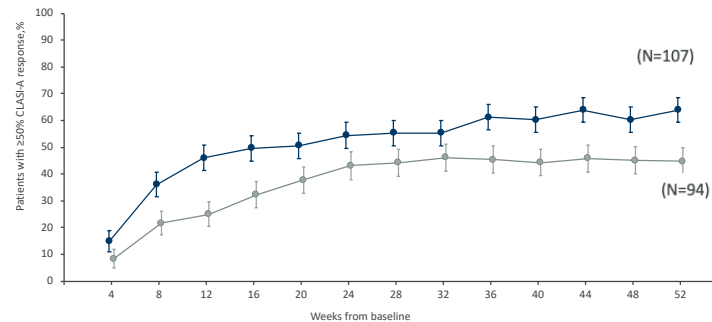


Week 52 treatment difference: 16.3
95% CI: 6.3%, 26.3%
p value: 0.001

anifrolumab placebo

**Early and sustained reduction
in overall disease activity**

Pooled TULIP 1/2 Phase III trials Skin CLASI⁶ response

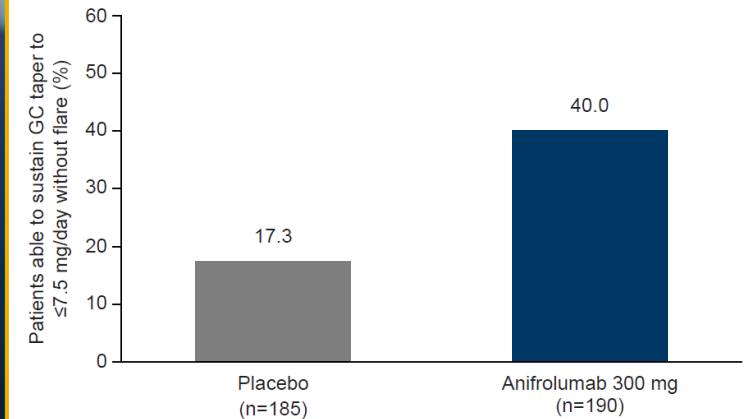


Subset of patients ≥ 10 CLASI-A score at baseline.
≥50% CLASI-A response at Week 12
treatment difference: 21.0% (95% CI: 8.1%, 34.0%);
nominal p<0.001

anifrolumab placebo

**Improves key organs of interest,
including reduction in skin activity**

Pooled TULIP 1/2 Phase III trials OCS sparing without flares



Subset of patients taking
≥ 10mg OCS per day at baseline.

anifrolumab placebo

**Prevents flares while also
allowing patients to taper OCS**

Source: Morand E et al, ACR 2019; Late breaking abstract L17. 1. Systemic lupus erythematosus 2. Mechanism of action 3. Lupus nephritis 4. Cutaneous lupus erythematosus 5. British Isles Lupus Assessment Group–based Composite Lupus Assessment.

Source: Werth et al. ACR 2020. Abstract ID: 0985 6. Cutaneous Lupus Erythematosus Disease Area and Severity Index.

Source: Furie et al. ACR 2020. Abstract ID: 1827.



Full pipeline and news flow

Upcoming milestones and key readouts

Respiratory and Immunology: near-term opportunities

Phase II	Phase III		Regulatory review
anifrolumab Type I IFN ¹ receptor lupus nephritis	AZD7442 long-acting antibody combination COVID-19 ⁶	<i>Fasenra</i> MANDARA IL5R EGPA ¹⁴	anifrolumab TULIP Type I IFN receptor SLE
anifrolumab Type I IFN receptor SLE subcutaneous	brazikumab IL23 Crohn's disease	<i>Fasenra</i> MESSINA IL5R eosinophilic oesophagitis	
brazikumab IL23 ² ulcerative colitis	nirsevimab⁷ mAb ⁸ -YTE ⁹ passive RSV ¹⁰ immunisation	<i>Fasenra</i> NATRON IL5R hypereosinophilic syndrome	
<i>Fasenra</i> ARROYO IL5R ³ chronic spontaneous urticaria	PT027¹¹ ICS/SABA asthma	<i>Fasenra</i> OSTRO, ORCHID IL5R nasal polyps	
<i>Fasenra</i> HILLIER IL5R atopic dermatitis	tezepelumab TSLP severe asthma	<i>Fasenra</i> RESOLUTE IL5R COPD	
tezepelumab⁴ TSLP ⁵ atopic dermatitis	Breztri LABA ¹² /LAMA ¹³ /ICS asthma	<i>Fasenra</i> FJORD IL5R bullous pemphigoid	
tezepelumab TSLP COPD			

Highlighted in presentation
 Other pipeline medicines

Upcoming milestones

H1 2021

- tezepelumab - severe asthma: regulatory submission
- *Fasenra* – nasal polyps: regulatory submission

H2 2021

- anifrolumab - lupus: regulatory decision (US, EU, JP)
- PT027 - asthma: Phase III data readout

2022

- *Fasenra* - eosinophilic oesophagitis, hypereosinophilic syndrome: Phase III data readout

Status as of 25 March 2021. 1. Interferon 2. Interleukin 23 3. Interleukin 5 receptor 4. In collaboration with Amgen Inc. 5. Thymic stromal lymphopoietin 6. Coronavirus disease 2019 9. 7. In collaboration with Sanofi S.A. 8. Monoclonal antibody 9. Triple modification, M252Y/S254T/T256E, of the fragment crystallisable region of an IgG antibody which extends half life - Robbie, G.J., et al. *Antimicrob Agents Chemother*, 2013. 57(12): p. 6147-53 10. Respiratory syncytial virus 11. In collaboration with Avillion 12. Long acting beta agonist 13. Long acting muscarinic agonist 14. Eosinophilic granulomatosis with polyangiitis.



Questions & Answers

To ask a question

Webinar

Click 'Raise Hand' (preferred):



or type your question into the Q&A box
(alternative)

Phone

*6 - Toggle mute/unmute

*9 - Raise hand



Appendix



Publications

anifrolumab				
Trial	Congress/journal	Title	Author	Citation
TULIP 1 and 2	European League Against Rheumatism (EULAR) 2020, <i>Annals of the Rheumatic Diseases</i>	Oral Presentation: Early and sustained responses with anifrolumab treatment in patients with active systemic lupus erythematosus (SLE) in 2 phase 3 trials	Morand EF, Furie R, Bruce I, et al.	2020;79(suppl. 1):2-3.
TULIP 1 and 2	EULAR 2020, <i>Annals of the Rheumatic Diseases</i>	Oral Presentation: Efficacy of anifrolumab in active systemic lupus erythematosus: patient subgroup analysis of BICLA response in 2 phase 3 trials	Morand EF, Furie R, Tanaka Y, et al.	2020;79(suppl. 1):32.
TULIP 1 and 2	American College of Rheumatology (ACR) 2020, <i>Arthritis & Rheumatology</i>	Oral Presentation: Early and sustained reduction in severity of skin disease with anifrolumab treatment in patients with active SLE measured by the Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI): pooled data from 2 phase 3 studies	Werth V, Furie R, Morand E, et al.	2020; 72 (suppl. 10).
Breztri				
ETHOS	British Thoracic Society (BTS) 2021, <i>Thorax</i>	Oral Presentation: Rate of Severe COPD Exacerbations with Budesonide/Glycopyrronium/Formoterol Fumarate Dihydrate Metered Dose Inhaler (BGF MDI) Versus Dual Therapies: A Post-hoc Subgroup Analysis of the ETHOS trial	Ferguson G, Rabe K, Martinez F, et al.	2021;76:A16.
ETHOS	American Thoracic Society (ATS) 2020, <i>American Journal of Respiratory and Critical Care Medicine</i>	Oral Presentation: Single-Inhaler Triple Combination Therapy with Budesonide/Glycopyrrolate/Formoterol Fumarate Metered Dose Inhaler (BGF MDI) at Two Corticosteroid Dose Levels in COPD: ETHOS trial	Rabe KF, Martinez FJ, Ferguson GT, et al.	2020;201:2493.
ETHOS	European Respiratory Society (ERS) 2020, <i>European Respiratory Journal</i>	Poster: Exacerbation benefit by blood eosinophil counts with budesonide/glycopyrronium/formoterol metered dose inhaler (BGF MDI) at two ICS dose levels in the ETHOS trial: a subgroup analysis	Rabe KF, Martinez FJ, Ferguson GT, et al.	2020;56(suppl. 64):984.
ETHOS	ERS 2020, <i>European Respiratory Journal</i>	Poster: COPD exacerbation rates by month in the ETHOS trial with budesonide/glycopyrronium/formoterol metered dose inhaler (BGF MDI) at two ICS dose levels	Rabe KF, Martinez FJ, Ferguson GT, et al.	2020;56(suppl. 64):977.
ETHOS	ERS 2020, <i>European Respiratory Journal</i>	Oral Presentation: Seasonal variation in COPD exacerbation rates: budesonide/glycopyrronium/formoterol metered dose inhaler (BGF MDI) at two ICS dose levels in the ETHOS trial	Rabe KF, Martinez FJ, Ferguson GT, et al.	2020;56(suppl. 64):5238.
ETHOS	ERS 2020, <i>European Respiratory Journal</i>	Oral Presentation: COPD exacerbation benefits relative to pneumonia risk with budesonide/glycopyrronium/formoterol metered dose inhaler: analyses from ETHOS	Rabe KF, Martinez FJ, Ferguson GT, et al.	2020;56(suppl. 64):5230.



Publications, continued

Fasenra				
Trial	Congress/journal	Title	Author	Citation
PONENTE	American Academy of Allergy, Asthma & Immunology (AAAAI) 2021, <i>The Journal of Allergy and Clinical Immunology</i>	Poster: Elimination of Oral Corticosteroids (OCS) with (or Following) Benralizumab Treatment in OCS-Dependent Asthmatics Using a Rapid, Personalized Algorithm: The PONENTE Trial	Menzies-Gow A, Gurnell M, Heaney LG, et al.	2021;147(2 suppl.):AB249.
BORA	AAAAI 2020, <i>The Journal of Allergy and Clinical Immunology</i>	Oral Presentation: Three-Year Safety and Efficacy of Benralizumab for Adolescent Patients with Severe, Uncontrolled Asthma: Results of BORA Extension Study	Busse WW, Bleecker ER, FitzGerald JM, et al.	2020;145(2 suppl.):AB174.
ANDHI	American Thoracic Society (ATS) 2020, <i>American Journal of Respiratory and Critical Care Medicine</i>	Poster: Exacerbation Reduction and Early Improvements in SGRQ, Lung Function, and Symptoms of Nasal Polyposis with Benralizumab for Severe, Eosinophilic Asthma: Phase IIIb ANDHI Trial	Harrison TW, Chanez P, Menzella F, et al.	2020;201:A4274.
ANDHI	European Academy of Allergy and Clinical Immunology (EAACI), <i>Allergy</i>	Oral Presentation: Benralizumab Efficacy for Severe, Eosinophilic Asthma with a Diagnosis of Nasal Polyposis: Results from the Phase IIIb ANDHI Trial	Canonica GW, Harrison TW, Chanez P, et al.	2020;75(suppl. 109):114
OSTRO	American College of Allergy, Asthma and Immunology (ACAAI) 2020, <i>Annals of Allergy, Asthma & Immunology</i>	Poster: Comprehensive Response to Benralizumab by Patients with Nasal Polyposis and Severe, Eosinophilic Asthma	Kreindler J, Chanez P, Bourdin A, et al.	2020;125(5 suppl.):S29.
PT027				
MANDALA	ATS 2020, <i>American Journal of Respiratory and Critical Care Medicine</i>	Poster: Evaluation of the Efficacy and Safety of As-needed PT027 (budesonide/albuterol MDI) Compared to As-needed Albuterol MDI in Adults and Children 4 Years of Age or Older with Uncontrolled Moderate to Severe Asthma: Design of the MANDALA Study	Chipps BE, Albers FC, Reilly L, et al.	2020;201(suppl.):A3015.
tezepelumab				
NAVIGATOR	AAAAI 2021, <i>The Journal of Allergy and Clinical Immunology</i>	Poster: Efficacy and safety of tezepelumab in adults and adolescents with severe, uncontrolled asthma: results from the phase 3 NAVIGATOR study	Menzies-Gow A, Corren J, Bourdin A, et al.	2021;147(2 suppl.):AB249.
PATHWAY	AAAAI 2021, <i>The Journal of Allergy and Clinical Immunology</i>	Poster: Treatment with tezepelumab reduces serum interleukin (IL)-5 and IL-13 in patients with severe, uncontrolled asthma to levels approaching those observed in healthy individuals	Pham T-H, Cook B, Colice G, et al.	2021;147(2 suppl.):AB57.



Publications, continued

Tezepelumab, continued				
Trial	Congress/journal	Title	Author	Citation
PATHWAY	American Academy of Allergy, Asthma & Immunology (AAAAI) 2021, <i>The Journal of Allergy and Clinical Immunology</i>	Oral Presentation: Tezepelumab efficacy in patients with allergic and non-allergic asthma: a post hoc analysis of the PATHWAY phase 2b study	Corren J, Colice G, Salapa K, et al.	2021;147(2 suppl):AB157.
PATHWAY	AAAAI 2020, <i>The Journal of Allergy and Clinical Immunology</i>	Poster: Effect of Tezepelumab on Exacerbations in Patients with Severe, Uncontrolled Asthma, According to Baseline Body Mass Index: Results from the Phase 2b PATHWAY Study	Ambrose CS, Corren J, Salapa K, et al.	2020;145(2 Suppl):AB25
PATHWAY	American Thoracic Society (ATS) 2020, <i>American Journal of Respiratory and Critical Care Medicine</i>	Poster: The effect of tezepelumab on exacerbations in patients with severe, uncontrolled asthma according to baseline serum IL-5 and IL-13 levels: results from the phase 2b PATHWAY study	Corren J, Ambrose C, Salapa K, et al.	2020;201(Suppl):A4255.
PATHWAY	ATS 2020, <i>American Journal of Respiratory and Critical Care Medicine</i>	Poster: Seasonal variability of exacerbations in patients with severe, uncontrolled asthma and clinical benefits of tezepelumab: results from the PATHWAY phase 2b study	Corren J, Karpefors M, Hellqvist Å, et al.	2020;201(Suppl):A4257.
PATHWAY	ATS 2020, <i>American Journal of Respiratory and Critical Care Medicine</i>	Poster: Eosinophil counts and fractional exhaled nitric oxide levels after cessation of tezepelumab: results from the PATHWAY phase 2b study	Pavord I, Menzies-Gow A, Bengtsson T, et al.	2020;201(Suppl):A4255.
PATHWAY	ATS 2020, <i>American Journal of Respiratory and Critical Care Medicine</i>	Poster: Effects of tezepelumab on asthma exacerbations and type 2 biomarkers in patients with severe, uncontrolled asthma with and without nasal polyps: results from a post hoc analysis of the phase 2b PATHWAY study	Emson C, Corren J, Salapa K, et al.	2020;201(Suppl):A4256.
PATHWAY	European Respiratory Society (ERS) 2020, <i>European Respiratory Journal</i>	Poster: Efficacy of tezepelumab in patients with low and high bronchodilator reversibility in PATHWAY	Corren J, Liu MC, Bowen K, et al.	2020;56:2269.
PATHWAY	American College of Chest Physicians (CHEST) 2020, <i>Allergy and Airway</i>	Oral Presentation: The effect of tezepelumab on exacerbations in patients with severe, uncontrolled asthma according to baseline inhaled corticosteroid dose: results from the phase 2b PATHWAY study	Corren J, Ambrose CS, Salapa K, et al.	2020;158(4(suppl)):A30-A31.
PATHWAY	American College of Allergy, Asthma and Immunology (ACAAI) 2020, <i>Annals of Allergy, Asthma & Immunology</i>	Oral Presentation: Tezepelumab efficacy in severe asthma by specific allergen sensitivity: results from the PATHWAY study	Corren J, Ambrose CS, Salapa K, et al.	2020;125(5):S5-S6.



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