

Break-out session 3

Respiratory & Immunology: emerging pipeline

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25 March 2021

Interactive event for investors and analysts. This webinar is being recorded.
https://astrazeneca.zoom.us/webinar/register/WN_mahGJExaRViDh7sxJ6zlow



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Targeting diseases with great unmet medical need

Building on 50 years of respiratory care in immune-driven diseases



Asthma

>50%
patients remain
uncontrolled¹

~30%
patients considered
refractory to inhaled
corticosteroids²

339m patients³

broad access to treatment requires
both biologic and novel non-biologic
therapies



COPD⁴

3rd
leading cause of
death worldwide^{5,6}

>\$100bn
estimated annual
global burden⁷

0
treatments indicated to
slow or stop progression

0
new treatment modalities
for past 10 years



Immunology

5-7%
of people living with autoimmune
diseases, ranging from ultra-rare to
common⁸

70-90%
of patients not in remission on
current therapies for most
autoimmune diseases

~3-7%
annual increases in prevalence
of many autoimmune diseases^{9,10}

**Opportunities to build franchises
across many unmet needs**

1. Davis J, Trudo F, Siddall J, et.al., Burden of asthma among patients adherent to ICS/LABA: A real-world study, *Journal of Asthma*, 2019; 56:3, 332-340 2. AstraZeneca estimate 3. GINA, The Global Asthma Report 2018.

4. Chronic obstructive pulmonary disease 5 WHO, The top 10 causes of death [online] 6. GOLD, 2020 report 7. European Respiratory Society European Lung White Book.

8. <https://www.aarda.org/disease-list/> 9. including Crohn's disease, ulcerative colitis, atopic dermatitis and rheumatoid arthritis 10. Aaron Lerner et al. *International Journal of Celiac Disease*. Vol. 3, No. 4, 2015, pp 151-155.



Respiratory & Immunology: strategy

Disease modification and clinical remission

Diseases with great unmet need



Asthma



COPD



IPF¹



Cough



Rheumatological



Dermatological



Gastrointestinal

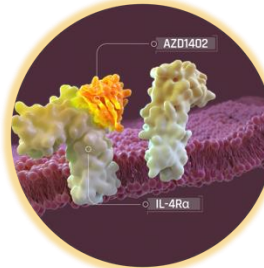


Osteoarthritis pain

Increased probability of success



Differentiated and unbiased novel targets

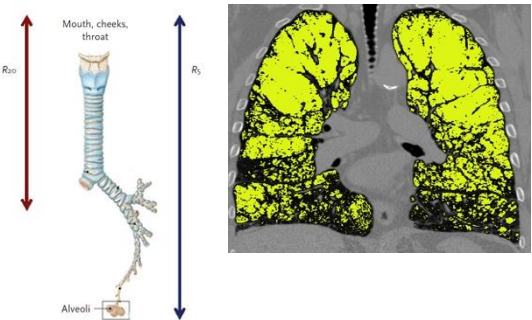


New modalities - nothing is undruggable



Precision medicine from the start

Transformative endpoints



Demonstrating disease modification: small airway function and imaging



Digital health



Patient-centricity

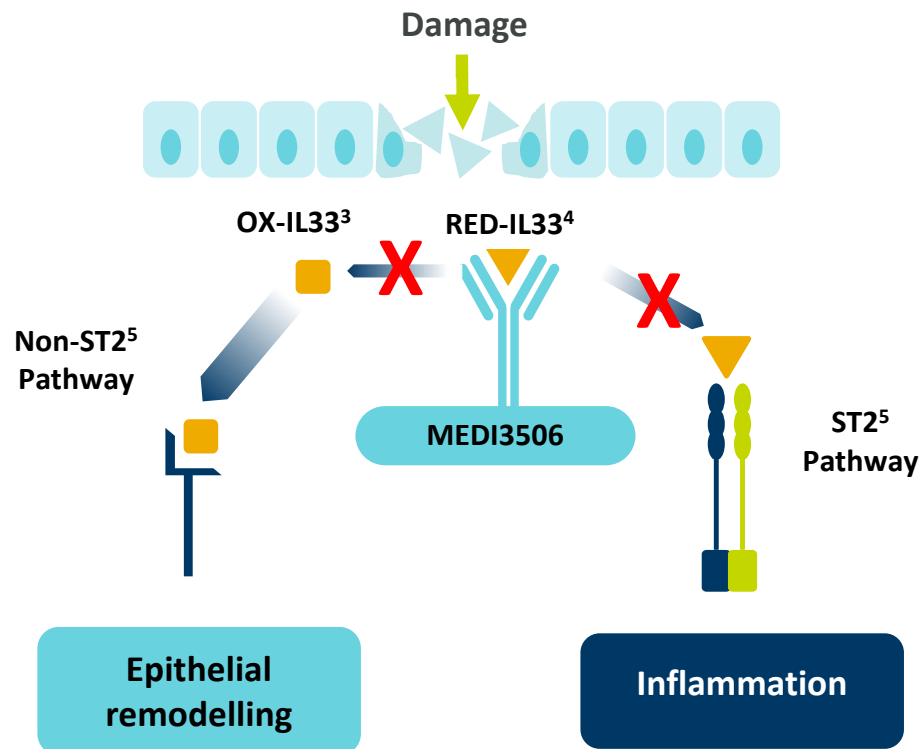
1. Idiopathic pulmonary fibrosis.



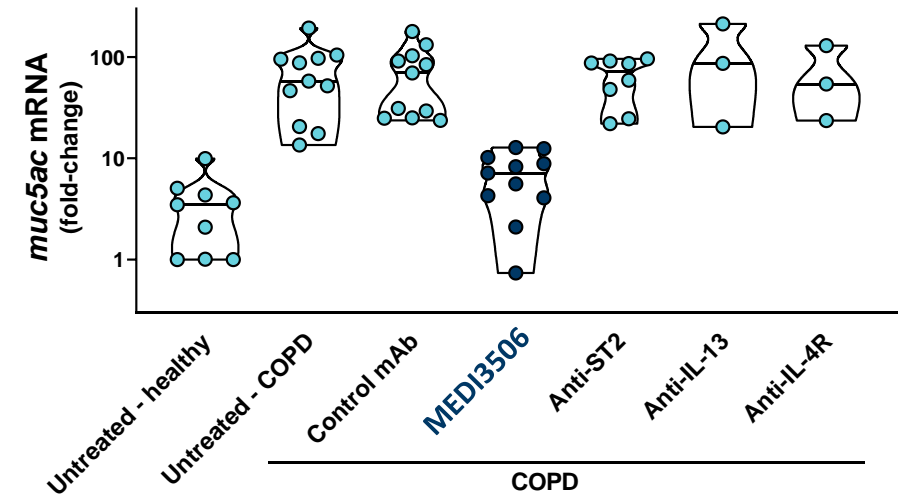
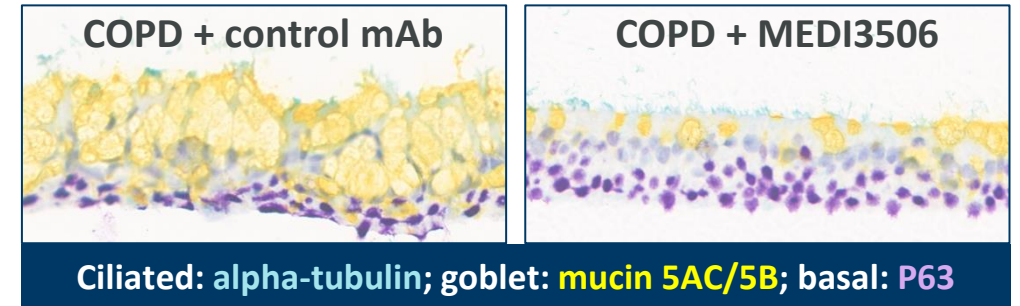
MEDI3506: IL33¹ mAb²

Targeting a broad-acting, damage-response epithelial cytokine

Disease-modification potential



Reverting the epithelial phenotype



1. Interleukin 33 2. monoclonal antibody 3. Oxidised IL33 4. Reduced IL33 5. ST2 (also known as IL1RL1, DER4, T1 and FIT-1) is a member of the toll-like/interleukin-1 receptor superfamily. Source: AstraZeneca data on file.

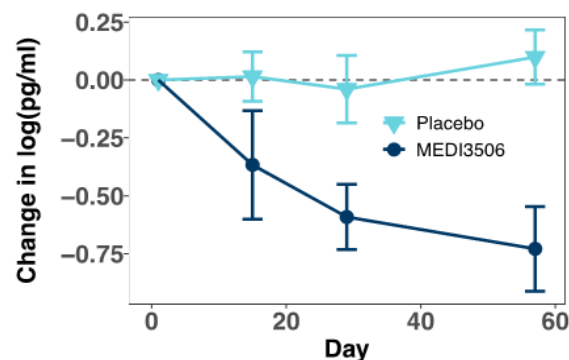
Source: AstraZeneca data on file.



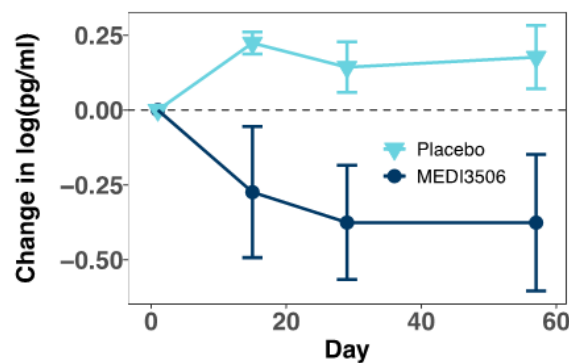
MEDI3506: IL33 mAb

Targeting a broad-acting, damage-response epithelial cytokine

Phase I: pharmacodynamic effects demonstrated in COPD¹



Serum
IL5²
reduction



Serum
IL13³
reduction

Phase II trials



COPD Phase II n=322 FPCD⁴: Q1 2021
Data anticipated: 2022



Asthma Phase II n=228 FPCD: Q4 2020
Data anticipated: 2022



Atopic dermatitis Phase II n=152 FPCD: Q4 2019
Data anticipated: H2 2021



Diabetic kidney disease Phase II n=565 FPCD: Q4 2019
Data anticipated: 2022



COVID-19 ACCORD⁵ Phase II n=120 FPCD: Q2 2020
Data anticipated: H1 2021

1. Mixed effect longitudinal modelling - MEDI3506 reduced serum IL5 and IL13 (p=0.0037 and 0.034, respectively). All plots show means +/- SEMs 2. Interleukin 5 3. Interleukin 13. Source: AstraZeneca data on file.

4. First patient commenced dosing 5. Sponsored by the UK Government's Therapeutics Taskforce.

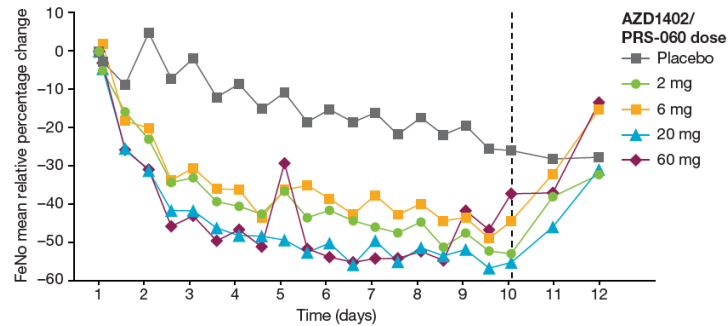


AZD1402¹: IL4Ra² and AZD0449: iJAK³

Addressing unmet need in asthma

Targeted approach following
precedented systemic biologic

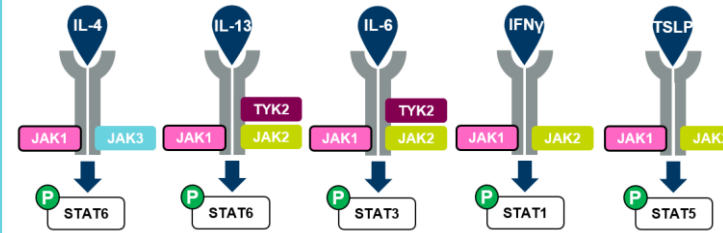
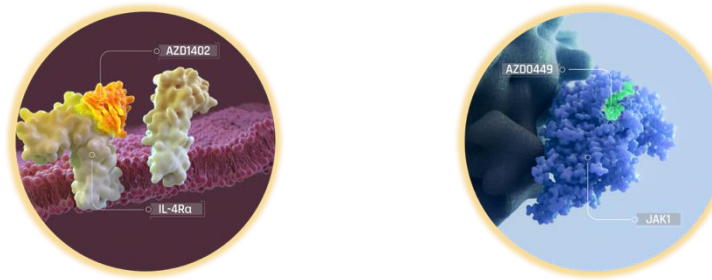
AZD1402



FeNO⁴, a biomarker of type-2
pulmonary inflammation

**Rapid inhibition of FeNO
in mild asthmatic patients**

Inhaled targeted biologics and
inhaled broader spectrum small
molecules



AZD0449

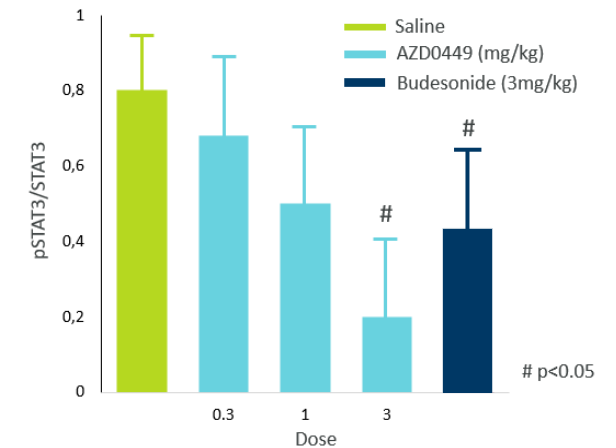
Broader anti-inflammatory effect

AZD1402
Type-2 endotype

Source: AstraZeneca data on file.

Opportunity for broader efficacy
across asthma endotypes

AZD0449



Inhibition of phosphorylation of
STAT3⁵ following OVA⁶ challenge

**Target engagement demonstrated
in rodent models of asthma**

5. Signal transducer and activator of transcription 6. Ovalbumin.
Source: AstraZeneca data on file.

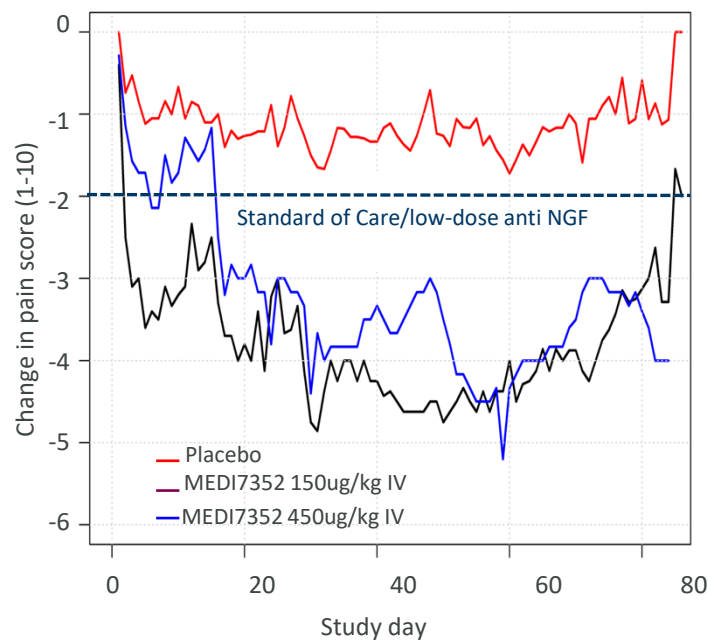
1. In collaboration with Pieris Pharmaceuticals Inc. 2. Interleukin 4 receptor alpha. 3. Inhaled janus kinase 4. Fractional exhaled nitric oxide. Source: Bruns et al., *European Respiratory Journal* 2019 54: PA3709.



MEDI7352: bispecific fusion protein specific for NGF¹ and TNF²

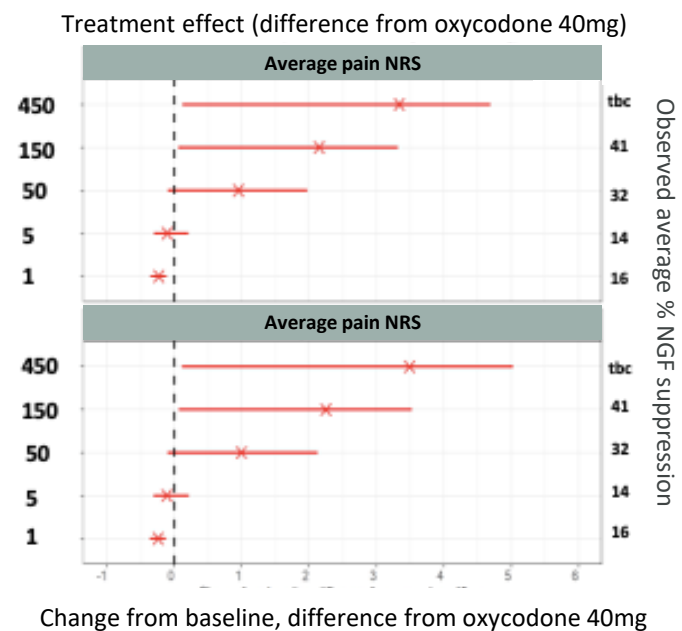
Potential synergy between blocking NGF and TNF in pain

Decreased daily pain scores in osteoarthritis patients



Peak reduction of c.3 points on a numerical rating scale vs. placebo

Modelling suggests significant efficacy at <50% NGF suppression



Lower levels of NGF suppression may be associated with a favourable safety profile

Phase I/II trials



Painful osteoarthritis of the knee
Phase I n=132
FPCD: Q1 2016
Data anticipated: H1 2021



Painful diabetic neuropathy
Phase II n=271
FPCD Q4 2018
Data anticipated: H2 2021



Painful osteoarthritis of the knee
Phase IIb n=300
Initiating
Data anticipated: 2022

1. Nerve growth factor 2. Tumour necrosis factor. Source: AstraZeneca data on file.

Source: AstraZeneca data on file.



Full pipeline and news flow

Upcoming milestones and expanding pipeline

Respiratory & Immunology: emerging pipeline

Phase I		Phase II	
AZD0284 RORγ ¹ psoriasis / respiratory	MEDI0618 PAR2 ⁴ antagonist mAb osteoarthritis pain	AZD1402 ⁷ inhaled IL4Ra asthma	MEDI3506 IL33 asthma
AZD0449 inhaled JAK inhibitor asthma	MEDI1341 ⁵ alpha synuclein Parkinson's disease	AZD7986 DPP1 ⁸ COPD	MEDI3506 IL33 COVID-19
AZD4041 ² orexin 1 receptor antagonist opioid use disorder	MEDI1814 ⁶ amyloid beta Alzheimer's disease	AZD9567 SGRM ⁹ chronic inflammatory diseases	MEDI7352 NGF/TNF osteoarthritis pain
AZD8154 inhaled PI3Kγ ³ asthma	AZD4604 inhaled JAK inhibitor asthma	MEDI3506 IL33 diabetic kidney disease	MEDI7352 NGF/TNF painful diabetic neuropathy
		MEDI3506 IL33 atopic dermatitis	navafenterol ¹⁰ MABA ¹¹ COPD
		MEDI3506 IL33 COPD	suvratoxumab alpha-toxin staphylococcus pneumonia

Highlighted in presentation
 Other pipeline medicines

Upcoming milestones

H1 2021

- MEDI3506 - multiple indications: Phase I data, Phase II data
- AZD1402 - asthma: Phase II start
- AZD0449 - asthma: Phase II start
- MEDI7352 - pain: Phase I data, Phase II start, Phase II data
- AZD4604 - asthma: Phase I start

H2 2021

- MEDI3506 - multiple indications: Phase II data
- MEDI7352 - pain: Phase II data

Status as of 25 March 2021. 1. Retinoid-related orphan nuclear receptor gamma 2. In collaboration with Eolas Therapeutics Inc. and NIH 3. Phosphatidylinositol 3-kinase gamma delta 4. Protease-activated receptor-2 5. In collaboration Takeda Pharmaceutical Company Ltd. 6. In collaboration with Eli Lilly and Company 7. In collaboration with Pieris Pharmaceuticals Inc. 8. Dipeptidyl-peptidase 1 9. Selective glucocorticoid receptor modulator 10. In collaboration with Almirall 11. Muscarinic antagonist beta2-agonist.



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



Publications

MEDI3506				
Trial	Congress/journal	Title	Author	Citation
Pre-clinical	British Thoracic Society (BTS) Winter Meeting 2021	The pharma perspective – what can academia do (and do we need any new drugs)?	Belvisi, M.G.	Available at: https://btswinter.online-event.co/login
Pre-clinical	Keystone eSymposia 2020: Asthma: New Discoveries and Therapies in the Age of COVID	Asthma Therapeutics: Now and Future Directions	Belvisi, M.G.	Available at: https://virtual.keystonesymposia.org/ks/live/683/page/6431#sessionCollapse4773
AZD0449				
Pre-clinical	European Respiratory Society (ERS) 2020: <i>European Respiratory Journal</i>	Poster: Profiling the impact of two JAK inhibitors in a pre-clinical model of allergic asthma	Pinkerton J, Dekkak B, Zervas D, et al	<i>European Respiratory Journal</i> 2020 56: 3302
AZD4606				
Pre-clinical	ERS 2020: <i>European Respiratory Journal</i>	Poster: Profiling the impact of two JAK inhibitors in a pre-clinical model of allergic asthma	Pinkerton J, Dekkak B, Zervas D, et al	<i>European Respiratory Journal</i> 2020 56: 3302
AZD1402				
Phase I	American Thoracic Society (ATS) 2019	Poster: First-in-human data for the inhaled IL-4Ra antagonist, AZD1402/PRS-060, reveals a promising clinical profile for the treatment of asthma.	Bruns IB, Fitzgerald M, Pardali K, et al.	<i>American Journal of Respiratory and Critical Care Medicine</i> 2020;201:A7476
Phase I	ERS 2019: <i>European Respiratory Journal</i>	Poster: Multiple ascending dose study of the inhaled IL-4Ra antagonist, AZD1402/PRS-060, in mild asthmatics demonstrates robust FeNO reduction and a promising clinical profile for the treatment of asthma.	Bruns IB, Fitzgerald MF, Mensing G, et al.	<i>European Respiratory Journal</i> 2019 54: PA3709
Phase I	ERS 2019: <i>European Respiratory Journal</i>	Oral presentation: Phase 1 evaluation of the inhaled IL-4Ra antagonist, AZD1402/PRS-060, a potent and selective blocker of IL-4Ra.	Bruns IB, Fitzgerald MF, Pardali K, et al.	<i>European Respiratory Journal</i> 2019 54: OA5336
AZD9567				
Phase I	<i>The Lancet Rheumatology</i>	Effects of a selective glucocorticoid receptor modulator (AZD9567) versus prednisolone in healthy volunteers: two phase 1, single-blind, randomised controlled trials.	Hegelund-Myrbäck T, Prothon S, Edman K, et al.	<i>Lancet Rheumatol</i> 2020; 2(1):e31-e41



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