Stock-exchange announcement
For media and investors only

Issued: 06 September 2024, London UK

GSK announces positive results from phase III trial of *Nucala* (mepolizumab) in COPD

- Primary endpoint met with a statistically significant and clinically meaningful reduction in annualised rate of moderate/severe exacerbations vs. placebo with data up to two years

---

GSK plc (LSE/NYSE: GSK) today announced positive headline results of MATINEE, the phase III clinical trial evaluating *Nucala* (mepolizumab), a monoclonal antibody that targets interleukin-5 (IL-5) in adults with chronic obstructive pulmonary disease (COPD).

The trial recruited COPD patients with broad clinical presentations of chronic bronchitis and/or emphysema, who were receiving optimised inhaled maintenance therapy. Participants were also required to have evidence of type 2 inflammation characterised by raised blood eosinophil count.[1] MATINEE met its primary endpoint with the addition of *Nucala* to inhaled maintenance therapy, and study results showed a statistically significant and clinically meaningful reduction in the annualised rate of moderate/severe exacerbations versus placebo with patients treated for up to 104 weeks.

The preliminary safety results are consistent with the known safety profile of *Nucala*. Further analysis of these data is ongoing.

COPD affects more than 300 million people globally with up to 40% of patients exhibiting type 2 inflammation characterised by raised blood eosinophil count, that drives exacerbations.[3,4] IL-5 is a key messenger protein (cytokine) in type 2 inflammation.[5] Recurrent exacerbations lead to damage to the lungs, progressive lung function decline and risk of hospitalisation. This can result in a vicious cycle of deterioration in overall physical health, which leads to worsening of symptoms and quality of life, and increased mortality.[6,7]

The full results of MATINEE will be presented at a future scientific congress and will inform ongoing discussions with regulatory authorities. *Nucala* is currently not indicated for COPD anywhere in the world.

About the mepolizumab development programme for COPD
The mepolizumab program in COPD is comprised of three clinical trials. The first two studies, METREX and METREO, completed in 2017. MATINEE was designed to supplement METREX and METREO, building on our learnings from these studies and IL-5 science to identify the patients who could benefit the most from *Nucala* and support future submissions and approvals for use in this indication.[3]

MATINEE is a multi-centre, randomised, placebo controlled, double-blind, parallel group study. The trial is designed to confirm the benefits of mepolizumab treatment on moderate or severe exacerbations in 806 COPD participants who were randomised to receive mepolizumab, or a placebo, as an add on to their optimised maintenance COPD therapy for at least 52 weeks and up to a maximum of 104 weeks.[1]

About *Nucala*
First approved in 2015 for severe asthma with an eosinophilic phenotype in the US, mepolizumab is a monoclonal antibody that targets and binds to interleukin-5 (IL-5), a key messenger protein (cytokine) in type 2 inflammation. *Nucala* has been developed for the treatment of a range of IL-5 mediated diseases associated with type 2 inflammation.

For product and important safety information please consult the country relevant summary of product characteristics. EU and UK available at: https://www.ema.europa.eu/en/documents/product-information/nucala-epar-product-information_en.pdf

About chronic obstructive pulmonary disease (COPD)
COPD is the third leading cause of death worldwide with exacerbations accounting for the greatest proportion of the total COPD burden on the healthcare system.[2,] Patients with COPD have chronic inflammation leading to persistent respiratory symptoms such as breathlessness and a productive cough. The daily impact on patients' lives can lead to anxiety and depression.[6] Exacerbations are acute episodes of worsening COPD symptoms and can result in hospitalisation, irreversible and cumulative lung damage or death.[6] Many patients continue to experience exacerbations despite standard treatment meaning that there is a need for targeted therapies that address the underlying pathobiology.[6,10,11] Up to 40% of patients have evidence of type 2 inflammation that drives exacerbations.[3,4] Blood eosinophil count is a biomarker for type 2 inflammation that can be easily measured by a simple blood test and indicates a patient's risk of exacerbation and deterioration, and response to treatment in COPD.[6] IL-5 is a core cytokine in type 2 inflammation. It is a major protein responsible for the growth, maturation, activation and survival of eosinophils, a type of white blood cell implicated in the pathogenesis of type 2 inflammatory diseases. Evidence indicates that IL-5 has an impact on other cell types beyond eosinophils, including those that contribute to inflammation, lung remodelling and disease progression.[12-16]

About GSK in respiratory
GSK continues to build on decades of pioneering work to deliver more ambitious treatment goals, develop the next generation standard of care, and redefine the future of respiratory medicine for hundreds of millions of people with respiratory diseases. With an industry-leading respiratory portfolio and pipeline of vaccines, targeted biologics and inhaled medicines, we are focused on improving outcomes and the lives of people living with all types of asthma and COPD along with less understood refractory chronic cough or rarer conditions like systemic sclerosis with interstitial lung disease. GSK is harnessing the latest science and technology with the aim to modify underlying disease dysfunction and prevent disease progression.

About GSK
GSK is a global biopharma company with a purpose to unite science, technology, and talent to get ahead of disease together. Find out more at gsk.com.

GSK enquiries

Media:	Tim Foley	+44 (0) 20 8047 5502	(London)
	Sarah Clements	+44 (0) 20 8047 5502	(London)
	Kathleen Quinn	+1 202 603 5003	(Washington DC)
	Lyndsay Meyer	+1 202 302 4595	(Washington DC)
Investor Relations:	Nick Stone	+44 (0) 7717 618834	(London)
	James Dodwell	+44 (0) 20 8047 2406	(London)
	Mick Readey	+44 (0) 7990 339653	(London)
	Josh Williams	+44 (0) 7385 415719	(London)
	Camilla Campbell	+44 (0) 7803 050238	(London)
	Steph Mountifield	+44 (0) 7796 707505	(London)
	Jeff McLaughlin	+1 215 751 7002	(Philadelphia)
	Frannie DeFranco	+1 215 751 4855	(Philadelphia)

Registered in England & Wales:
No. 3888792

Registered Office:
980 Great West Road
Brentford, Middlesex
TW8 9GS

References

1. ClinicalTrials.gov. Mepolizumab as Add-on Treatment IN Participants With COPD Characterized by Frequent Exacerbations and Eosinophil Level (MATINEE) Available at: https://clinicaltrials.gov/study/NCT04133909 Last accessed July 2024.
2. GBD 2019 Chronic Respiratory Diseases Collaborators. Global burden of chronic respiratory diseases and risk factors, 1990-2019: an update from the Global Burden of Disease Study 2019. *Lancet.* 2023:59;101936.
3. Singh D, et al. ECLIPSE Investigators. Eosinophilic inflammation in COPD: prevalence and clinical characteristics. *Eur Respir J.* 2014;44:1697-1700.
4. Saha S, *et al.* Eosinophilic airway inflammation in COPD. *Int J Chron Obstruct Pulmon Dis*. 2006;1(1):39-47.
5. Maspero J, et al. Type 2 inflammation in asthma and other airway diseases. *ERJ Open Res*. 2022;8:00576-2021.
6. GOLD Science Committee Members (2023-2024). The Global Strategy for Diagnosis, Management and Prevention of CO 2024. Available at: www.goldcopd.org Last accessed: July 2024
7. Hurst JR, et al. Susceptibility to Exacerbation in Chronic Obstructive Pulmonary Disease. *N Engl J Med*. 2010;363:1128-1138.
8. U.S. Food and Drug Administration. Nucala Full Prescribing Information. Available at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761122s000lbl.pdf. Last accessed December 2023.
9. European summary of product characteristics available at https://www.ema.europa.eu/en/documents/product-information/nucala-epar-product-information_en.pdf last accessed February 2023
10. Whittaker H, et al. Frequency and Severity of Exacerbations of COPD Associated with Future Risk of Exacerbations and Mortality: A UK Routine Health Care Data Study. *Int J Chron Obstruct Pulmon Dis*. 2022;17:427-437.
11. Rabe KF, et al. Targeting Type 2 Inflammation and Epithelial Alarmins in Chronic Obstructive Pulmonary Disease: A Biologics Outlook. *Am J Respir Crit Care Med*. 2023;208:396-405.
12. Buchheit KM, et al. Mepolizumab targets multiple immune cells in aspirin-exacerbated respiratory disease. *J Allergy Clin Immunol*. 2021;148(2):574-584.
13. Barretto KT, et al. Human airway epithelial cells express a functional IL-5 receptor. *Allergy*. 2020;75(8):2127-2130.
14. Bajbouj K, et al. IL-5 receptor expression in lung fibroblasts: Potential role in airway remodelling in asthma. *Allergy*. 2023;78(3):882-885.
15. Siddiqui S, et al. Eosinophils and tissue remodeling: Relevance to airway disease. *J Allergy Clin Immunol*. 2023;152(4):841-857.
16. Bergantini L, et al. Regulatory T cell monitoring in severe eosinophilic asthma patients treated with mepolizumab. *Scand J Immunol*. 2021;94(1):e13031.