Stock-exchange announcement
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Nucala (mepolizumab) delivers clinically meaningful and statistically significant reduction in COPD exacerbations, with positive MATINEE trial results published in *New England Journal of Medicine*

- 21% reduction in annualised rate of moderate/severe exacerbations in a wide COPD population
- 31% reduction in annualised rate of moderate/severe exacerbations in the sub-group of patients with chronic bronchitis only in post-hoc analysis
- 35% reduction in annualised rate of exacerbations leading to emergency department visit and/or hospitalisation secondary endpoint*

GSK plc (LSE/NYSE: GSK) today announced positive results for *Nucala* (mepolizumab) in the treatment of chronic obstructive pulmonary disease (COPD), with the full results from the MATINEE phase III trial published in the *New England Journal of Medicine.* The trial evaluated mepolizumab, a monoclonal antibody targeting interleukin-5 (IL-5), in a wide spectrum of patients with COPD, including the most severe and difficult to treat as categorised in the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines.[1] Patients recruited had evidence of type 2 inflammation, characterised by blood eosinophil count, and included those with chronic bronchitis, emphysema-only or both.[2] The monthly administration of mepolizumab demonstrated improvement across all exacerbation endpoints, which were maintained over the 2-year (up to 104 weeks) study period.[2]

In the full population studied, mepolizumab showed a clinically meaningful and statistically significant 21% reduction in the annualised rate of moderate/severe exacerbations versus placebo, meeting the primary endpoint for MATINEE (rate ratio [95% confidence interval (CI)]: 0.79 [0.66, 0.94]; P=0.011) (AER mepolizumab = 0.80 exacerbations per year versus placebo = 1.01) n= 804; mepolizumab = 403, placebo = 401).[2] In addition, mepolizumab also showed a 31% reduction in the annualised rate of moderate/severe exacerbations versus placebo in a post-hoc analysis of patients with clinician assessed chronic bronchitis only (rate ratio [95% CI]: 0.69 [0.51, 0.93] n=338: mepolizumab = 170, placebo = 168).[2]

A 35% reduction in the annualised rate of exacerbations leading to emergency department visits and/or hospitalisation was shown with mepolizumab versus placebo, a secondary endpoint of the MATINEE study (rate ratio [95% CI]: 0.65 [0.43, 0.96] nominally significant after adjustment for multiplicity) (AER mepolizumab = 0.13 exacerbations per year versus placebo = 0.20)). Mepolizumab is the only biologic with data that shows a reduction in emergency department visits and/or hospitalisation in a phase III trial. Reducing hospitalisations is a key goal of COPD management.[3] COPD-related hospitalisations are a major healthcare challenge and projected to become the number one cause of medical admissions.[4] If hospitalised due to COPD, one in ten patients will die during the stay, up to one in four over the next year and half will lose their lives within five years.[5,6]

Kaivan Khavandi, SVP, Global Head, Respiratory, Immunology & Inflammation R&D, GSK said: “Today’s MATINEE results show that mepolizumab can help prevent exacerbations, including those leading to emergency department visits and/or hospitalisation. These exacerbations are devastating for patients, known to cause irreversible lung damage, worsening of symptoms and increased mortality. For decades, we have and will continue to push the boundaries of innovation to prevent disease progression and make a meaningful impact on the lives of people affected by COPD.”

Frank Sciurba, Professor of Pulmonary, Allergy and Critical Care Medicine, and lead author of the MATINEE trial said: “Every physician will know the feeling of seeing a patient hospitalised due to an exacerbation that could have possibly been prevented. The MATINEE trial uncovers new possibilities in the treatment landscape for COPD

patients with type 2 inflammation, as we strive to target drivers of disease and improve the lives of patients suffering with COPD."

High response rates were observed in Patient Reported Outcomes (PROs) in the mepolizumab group, however there was no difference observed for St George's Respiratory Questionnaire (SGRQ), the COPD Assessment Test (CAT) and the Evaluating Respiratory Symptoms (E-RS) in the full study population versus placebo.[2] The incidence of adverse events were similar between mepolizumab and placebo (mepolizumab vs placebo: 74% vs 77%), with the most frequent being exacerbation or worsening of COPD (mepolizumab vs placebo: 12% vs 15%) and COVID-19 infection (12% vs 12%).[2]

Nucala is not approved for the treatment of COPD in any country. Regulatory submissions are under review in several countries, including the US, China and the EU. The US FDA has provided a PDUFA date of May 7, 2025.

*Nominally significant after adjustment for multiplicity

About MATINEE
MATINEE is a phase III, randomised (1:1), double-blind, parallel-group trial assessing the efficacy and safety of mepolizumab 100 mg as add-on therapy, administered subcutaneously every 4 weeks for 52–104 weeks, versus placebo in addition to optimal inhaled triple therapy (dual long-acting bronchodilators plus inhaled corticosteroid).[2]

Positive results were achieved in a wide population of patients with COPD. The efficacy and safety of mepolizumab was assessed in patients with COPD with evidence of type 2 inflammation, characterised by a blood eosinophil count (≥300 cells/µL). Patients could participate with a range of clinical presentations of COPD including chronic bronchitis, emphysema only or a combination of both. The condition of patients ranged in severity from moderate to very severe, or stages 2-4 as assessed by the medically recognised scale of Global Initiative for Chronic Obstructive Lung Disease (GOLD).[2] The full analysis of MATINEE included 403 patients enrolled on the mepolizumab arm and 401 on placebo, all of whom had experienced exacerbations in the previous year despite receiving optimised inhaled maintenance therapy.[2]

About chronic obstructive pulmonary disease (COPD) and type 2 inflammation
COPD is a progressive and heterogeneous inflammatory lung disease that includes chronic bronchitis and/or emphysema.[3] It affects more than 390 million people globally and is the third leading cause of death.[7,8] Patients with COPD experience persistent respiratory symptoms such as breathlessness, cough, and sputum along with progressive airflow obstruction due to the chronic inflammation, that impact daily life.[3] Type 2 inflammation is present in a variety of immuno-inflammatory conditions and is a major contributor to symptoms and exacerbations in up to 40% of people with COPD.[2,9]

Despite inhaled triple therapy, many patients experience persistent symptoms and exacerbations.[10] Exacerbations are acute episodes of worsening COPD symptoms, which can result in hospitalisation and irreversible lung damage.[3] Early intervention is important in preventing exacerbations and cumulative lung damage.[3]

About *Nucala*
Nucala 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. It is currently approved for use in the US and Europe across four IL-5 mediated conditions. *Nucala* is currently not indicated for COPD in any country.

For product and important safety information please consult the country relevant summary of product characteristics. EU available at: https://www.ema.europa.eu/en/documents/product-information/nucala-epar-product-information_en.pdf. The US prescribing information is available at: NUCALA-PI-PIL-IFU-COMBINED.PDF.

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 of modifying the underlying disease dysfunction and preventing progression.

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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.

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Cautionary statement regarding forward-looking statements
GSK cautions investors that any forward-looking statements or projections made by GSK, including those made in this announcement, are subject to risks and uncertainties that may cause actual results to differ materially from those projected. Such factors include, but are not limited to, those described in the "Risk Factors" section in GSK's Annual Report on Form 20-F for 2024, and GSK's Q1 Results for 2025.

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