Stock-exchange announcement
For media and investors only

Issued: 22 May 2025, Philadelphia, PA

Nucala (mepolizumab) approved by US FDA for use in adults with chronic obstructive pulmonary disease (COPD)

- *Nucala* is the only approved biologic studied in a wide COPD population with an eosinophilic phenotype characterized by blood eosinophil count (BEC) starting at 150 cells/µL
- Approval based on the positive MATINEE and METREX phase III trials
- MATINEE data included reduction of exacerbations leading to hospitalization and/or emergency department visits
- Nearly 70% of patients in the US who are inadequately controlled on inhaled triple therapy have a BEC ≥150 cells/µL

GSK plc (LSE/NYSE: GSK) today announced that the US Food and Drug Administration (FDA) has approved *Nucala* (mepolizumab) as an add-on maintenance treatment for adult patients with inadequately controlled COPD and an eosinophilic phenotype.

FDA's approval was based on data from the positive MATINEE and METREX phase III trials. Across these trials, mepolizumab showed a clinically meaningful and statistically significant reduction in the annualized rate of moderate/severe exacerbations versus placebo in a wide spectrum of COPD patients with an eosinophilic phenotype.[1,2] Preventing exacerbations is a key goal of COPD management.[3] Exacerbations are devastating for patients, known to cause irreversible lung damage, worsening of symptoms and increased mortality.[3] The incidence of adverse events was similar between placebo and mepolizumab groups.[1,2]

Mepolizumab is the only approved biologic evaluated in patients with an eosinophilic phenotype characterized by a blood eosinophil count (BEC) threshold as low as ≥150 cells/µL.[1,2] BEC is captured by a simple blood test that measures levels of eosinophils, a type of white blood cell which is a biomarker for type 2 inflammation and indicates a patient's risk of exacerbation.[3] Approximately 70% of COPD patients in the US who are inadequately controlled on inhaled triple therapy and continue to exacerbate have a BEC starting at 150 cells/µL and above.[4,5] This represents over a million people at risk of exacerbations, including those leading to emergency department (ED) visits and/or hospitalizations, who could add mepolizumab as an option to their COPD treatment.[4,5]

Kaivan Khavandi, SVP, Global Head, Respiratory, Immunology & Inflammation R&D, GSK, said: "The approval of *Nucala* in the US provides an important option for COPD patients. Long-term follow-up studies have demonstrated that exacerbations are the single most important predictor of future risk, with particularly poor outcomes in those requiring hospital visits or admissions. Today there is hope for improved care for COPD patients with an eosinophilic phenotype, including those with a BEC threshold as low as ≥150 cells/µL who need new options like *Nucala* to support their treatment journey."

Jean Wright, MD, MBA, Chief Executive Officer of the COPD Foundation said: "COPD isn't just a disease, it's a relentless cycle. For individuals living with COPD, managing exacerbations is an ongoing challenge, even with inhaled maintenance therapy. Biologics like mepolizumab are providing renewed optimism for those affected by COPD."

In both MATINEE and METREX trials, mepolizumab demonstrated a statistically significant reduction in the annualized rate of moderate or severe exacerbations compared with placebo, in patients with an eosinophilic phenotype, when added to triple inhaled therapy (MATINEE: rate ratio [RR], 0.79; 95% confidence interval [CI], 0.66 to 0.94; P=0.01) (METREX: rate ratio, 0.82; 95% CI, 0.68 to 0.98; adjusted P=0.04).[1,2] In a pre-defined secondary

endpoint in MATINEE, the annualized rate of COPD exacerbations requiring ED visits and/or hospitalization was reduced in the mepolizumab group when compared with placebo (rate ratio [RR] of 0.65; 95% CI: 0.43, 0.96 [not statistically significant due to a failure of an endpoint higher in the pre-defined statistical testing hierarchy]).[1] COPD-related hospitalizations are a major healthcare challenge and are projected to become the number one cause of medical admissions.[6] Emergency department visits and inpatient care already account for a large proportion of the annual direct medical costs of COPD, costing the US healthcare system around $7 billion a year.[7]

Mepolizumab is currently not approved for use in COPD in any other country. Regulatory submissions are under review in China and Europe.

About MATINEE and METREX

Both MATINEE and METREX are phase III, randomized (1:1), double-blind, parallel-group trials assessing the efficacy and safety of mepolizumab 100 mg as add-on therapy, administered subcutaneously every 4 weeks versus placebo in addition to optimal inhaled triple therapy (dual long-acting bronchodilators plus inhaled corticosteroid).[1,2]

MATINEE assessed the efficacy and safety of mepolizumab for 52–104 weeks, in 804 patients with COPD with evidence of type 2 inflammation, characterized 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 recognized scale of Global Initiative for Chronic Obstructive Lung Disease (GOLD). 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 optimized inhaled maintenance therapy.[1]

The full study results from MATINEE were recently published in the *New England Journal of Medicine* with further data presented at the 2025 American Thoracic Society International Congress, including additional sub-analyses in patients with or without cardiovascular comorbidities, varying severities of prior exacerbations, and those with chronic bronchitis, emphysema-only or both.[1]

In METREX, the efficacy and safety of mepolizumab was evaluated for 52 weeks in 836 patients randomized (1:1) to mepolizumab or placebo across two groups, the eosinophilic phenotype group (blood eosinophil count of ≥150 cells/µl at study entry or ≥ 300 cells/µl within the past year) or the non-eosinophilic phenotype group (blood eosinophil count of <150 cells/µl at study entry and no evidence of ≥300 cells/µl within the past year).
The study results from METREX were published in 2017 in *the New England Journal of Medicine*.[2]

About 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 14 million people in the US with more than 300,000 hospitalizations and more than 900,000 emergency department visits each year.[8,9] 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]

Despite inhaled triple therapy, many patients experience persistent symptoms and exacerbations.[10] Exacerbations are acute episodes of worsening COPD symptoms, which can result in hospitalization 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 Europe across four IL-5 mediated conditions and in the US across five such conditions.

The US Prescribing Information is available at NUCALA-PI-PIL-IFU-COMBINED.PDF

NUCALA is indicated for the:

- add-on maintenance treatment of adult and pediatric patients aged 6 years and older with severe asthma and with an eosinophilic phenotype. NUCALA is not indicated for the relief of acute bronchospasm or status asthmaticus.
- add-on maintenance treatment of chronic rhinosinusitis with nasal polyps (CRSwNP) in adult patients aged 18 years and older with inadequate response to nasal corticosteroids.
- add-on maintenance treatment of adult patients with inadequately controlled chronic obstructive pulmonary disease (COPD) and an eosinophilic phenotype. NUCALA is not indicated for the relief of acute bronchospasm.
- treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA).
- treatment of adult and pediatric patients aged 12 years and older with hypereosinophilic syndrome (HES) for ≥6 months without an identifiable non-hematologic secondary cause.

Important Safety Information for NUCALA

CONTRAINDICATIONS
Known hypersensitivity to mepolizumab or excipients.

WARNINGS AND PRECAUTIONS
Hypersensitivity Reactions
Hypersensitivity reactions (eg, anaphylaxis, angioedema, bronchospasm, hypotension, urticaria, rash) have occurred with NUCALA. These reactions generally occur within hours of administration but can have a delayed onset (ie, days). Discontinue if a hypersensitivity reaction occurs.

Acute Symptoms of Asthma or COPD or Acute Deteriorating Disease
NUCALA should not be used to treat acute symptoms or acute exacerbations of asthma or COPD, or acute bronchospasm.

Opportunistic Infections: Herpes Zoster
Herpes zoster infections have occurred in patients receiving NUCALA. Consider vaccination if medically appropriate.

Reduction of Corticosteroid Dosage
Do not discontinue systemic or inhaled corticosteroids abruptly upon initiation of therapy with NUCALA. Decreases in corticosteroid doses, if appropriate, should be gradual and under the direct supervision of a physician. Reduction in corticosteroid dose may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy.

Parasitic (Helminth) Infection
Treat patients with pre-existing helminth infections before initiating therapy with NUCALA. If patients become infected while receiving NUCALA and do not respond to anti-helminth treatment, discontinue NUCALA until infection resolves.

ADVERSE REACTIONS
Most common adverse reactions (≥5%):
- Severe asthma trials: headache, injection site reaction, back pain, fatigue
- CRSwNP trial: oropharyngeal pain, arthralgia
- COPD trials: back pain, diarrhea, cough
- EGPA and HES trials (300 mg of NUCALA): most common adverse reactions were similar to severe asthma

Systemic reactions, including hypersensitivity, occurred in clinical trials in patients receiving NUCALA. Manifestations included rash, pruritus, headache, myalgia, flushing, urticaria, erythema, fatigue, hypertension, warm sensation in trunk and neck, cold extremities, dyspnea, stridor, angioedema, and multifocal skin reaction. A majority of systemic reactions were experienced the day of dosing.

USE IN SPECIFIC POPULATIONS

The data on pregnancy exposures are insufficient to inform on drug-associated risk. Monoclonal antibodies, such as mepolizumab, are transported across the placenta in a linear fashion as the pregnancy progresses; therefore, potential effects on a fetus are likely to be greater during the second and third trimesters.

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, GSK is 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.

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)
	Dan Smith	+44 (0) 20 8047 5502	(London)
	Kathleen Quinn	+1 202 603 5003	(Washington DC)
	Lyndsay Meyer	+1 202 302 4595	(Washington DC)
Investor Relations:	Constantin Fest	+44 (0) 7831 826525	(London)
	James Dodwell	+44 (0) 20 8047 2406	(London)
	Mick Readey	+44 (0) 7990 339653	(London)
	Steph Mountifield	+44 (0) 7796 707505	(London)
	Jeff McLaughlin	+1 215 751 7002	(Philadelphia)
	Frannie DeFranco	+1 215 751 3126	(Philadelphia)

Registered in England & Wales:
No. 3888792

Registered Office:
79 New Oxford Street
London
WC1A 1DG

References

1. Sciurba F, et al. Mepolizumab to prevent exacerbations in COPD with an eosinophilic phenotype. *N Engl J Med.* Apr 2025;392:1710-1720. Available at nejm.org.
2. Pavord ID, et al. Mepolizumab for Eosinophilic Chronic Obstructive Pulmonary Disease. *N Engl J Med*. Oct 2017;377:1613-1629. DOI: 10.1056/NEJMoa1708208.
3. Global Initiative for Chronic Obstructive Lung Disease (GOLD). 2025 Gold Report. Available at: goldcopd.org. Last accessed May 2025.
4. GSK, Optum Analysis DOF (DOF 2024N562932_00).
5. Müllerová H, et al. Exacerbations and health care resource use among patients with COPD in relation to blood eosinophil counts. *Int J Chron Obstruct Pulmon Dis*. 2019;14:683-692. DOI: 10.2147/COPD.S194367.
6. Khakban A, et al. The Projected Epidemic of Chronic Obstructive Pulmonary Disease Hospitalizations over the Next 15 Years. A Population-based Perspective. *Am J Respir Crit Care Med*. 2017;195(3):287-291. DOI: 10.1164/rccm.201606-1162PP.
7. American Lung Association (ALA). COPD Trends Brief – Burden. Available at: Lung.org. Last accessed: May 2025.
8. American Lung Association. COPD Trends Brief – Burden. Available at: https://www.lung.org/research/trends-in-lung-disease/copd-trends-brief/copd-burden Last accessed: May 2025.
9. National Heart, Lung and Blood Institute. What is COPD? Available at: nhlbi.nih.gov/health/copd. Last accessed May 2025.
10. Chen S, Miravitlles M, Rhee CK, et al. Patients with Chronic Obstructive Pulmonary Disease and Evidence of Eosinophilic Inflammation Experience Exacerbations Despite Receiving Maximal Inhaled Maintenance Therapy. Int J Chron Obstruct Pulmon Dis. 2022 Sep 9;17:2187–2200. DOI: 10.2147/COPD.S378649.