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Nucala (mepolizumab) application for COPD accepted for review in China

- Around 100 million people live with COPD in China, accounting for almost 25% of all COPD cases globally
- Submission based on data from MATINEE trial, which showed a significant and clinically meaningful reduction in rate of moderate/severe exacerbations with *Nucala* compared to placebo
- Data includes positive results in the broadest COPD population studied with a biologic, including those with chronic bronchitis, emphysema only, or both
- *Nucala* could be the first approved biologic with monthly dosing for patients with COPD

GSK plc (LSE/NYSE: GSK) today announced that the China National Medical Products Administration has accepted for review the new drug application for the use of *Nucala* (mepolizumab), a monoclonal antibody that targets interleukin-5 (IL-5), as add-on maintenance treatment for patients with chronic obstructive pulmonary disease (COPD) with an eosinophilic phenotype.

IL-5 is a key cytokine (protein) in type 2 inflammation which is an underlying driver in many diseases. [2-4] This type of inflammation is detected in up to 40% of patients with COPD and is a major cause of symptoms and exacerbations that can lead to hospitalisation and/or emergency room visits.[2-4]

COPD affects more than 390 million people globally, with research estimating that approximately 100 people in China live with COPD, which accounts for almost 25% of the global COPD cases.[5,6] This puts a significant burden on healthcare resources and the lives of patients, with recurrent exacerbations accounting for a large proportion of the annual direct medical costs of COPD due to emergency department visits and inpatient care.[5-7] This burden is expected to dramatically increase due to the rapidly aging population in China.[6,7]

Nucala's application was supported by results from the positive Phase III MATINEE trial which showed a significant and clinically meaningful reduction in rate of moderate/severe exacerbations with *Nucala* compared to placebo. The trial recruited a wide spectrum of COPD patients including those with chronic bronchitis, emphysema-only or both.[1] These data indicate that *Nucala,* in addition to inhaled maintenance therapy, offers a clinically meaningful benefit to a patient population in need of treatments to reduce their risk of exacerbations.

If approved, *Nucala* could be the first approved biologic with monthly dosing for patients with COPD.

Nucala is currently approved for use in the China across three IL-5 mediated conditions. These include two respiratory indications as an add-on maintenance treatment for severe eosinophilic asthma in adults and adolescents aged 12 years and older and as an add-on therapy with intranasal corticosteroids for the treatment of adult patients with chronic rhinosinusitis with nasal polyps for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control. Indications also include the use of *Nucala* for the treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA).

Nucala is currently not approved for use in COPD in any country.

About the *Nucala* development programme for COPD
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.[8] *Nucala* has been developed for the treatment of a range of IL-5 mediated diseases associated with type 2 inflammation.[8]

The mepolizumab programme 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.[9]

MATINEE is a phase 3, randomized (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 inhaled triple therapy (dual long-acting bronchodilators plus inhaled corticosteroid) in 804 patients with COPD, a history of exacerbations, and evidence of type 2 inflammation characterised by raised blood eosinophil count.[1]

The primary endpoint was met with the addition of *Nucala* to inhaled maintenance therapy, showing a statistically significant and clinically meaningful reduction in the annualised rate of moderate/severe exacerbations versus placebo with patients treated for 52-104 weeks.

Data from MATINEE will be presented at a future scientific congress or in a peer reviewed journal. Global regulatory submissions including MATINEE data are ongoing.

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

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. It affects more than 390 million people globally and is the third leading cause of death resulting in more than 3 million deaths annually.[5,10] 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.[10]

Exacerbations are acute episodes of worsening COPD symptoms and can result in hospitalisation and irreversible lung damage that leads to progressive lung function decline.[10-12] Recurrent exacerbations accelerate disease progression and further increase the risk of hospitalisation adding to pressures on healthcare systems through emergency department visits and inpatient care.[10-12] For patients 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.[10-12]

Despite inhaled triple therapy, many patients experience persistent symptoms and exacerbations meaning there is a need for targeted therapies to address the underlying pathophysiology linked to disease progression.[10-13] Permanent and irreversible tissue damage seen in patients with advanced disease make it challenging to provide further improvements in respiratory symptoms and quality of life and is the reason why early intervention is so important in preventing exacerbations and cumulative lung damage.[10]

There is evidence to show IL-5 has broad effects on other structural and immune and cell types beyond eosinophils, and how they contribute to inflammation, which can lead to lung remodelling and disease progression.[2,3,14-18] Ongoing research is generating further evidence to understand the roles of these cells and their potential contribution to clinical outcomes in patients with respiratory diseases. Type 2 inflammation drives the underlying dysfunction of various immune-mediated conditions. IL-5 is a key cytokine (protein) in type 2 inflammation.[2-4] The presence of type 2 inflammation can be detected by blood eosinophil count, which measures the level of a type of white blood cell.[2-4]

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.

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References

1. ClinicalTrials.gov. Mepolizumab as Add-on Treatment IN Participants With COPD Characterized by Frequent Exacerbations and Eosinophil Level. Available at: https://clinicaltrials.gov/study/NCT04133909 Last accessed February 2025
2. Saha S, et al. Eosinophilic airway inflammation in COPD. *Int J Chron Obstruct Pulmon Dis*. 2006;1(1):39-47.
3. Maspero J, et al. Type 2 inflammation in asthma and other airway diseases. *ERJ Open Res*. 2022;8:00576-2021.
4. Singh D, et al. Eosinophilic inflammation in COPD: prevalence and clinical characteristics. *Eur Respir J*. 2014;44:1697-1700.
5. Adeloye D, et al. NIHR RESPIRE Global Respiratory Health Unit. Global, regional, and national prevalence of, and risk factors for, chronic obstructive pulmonary disease (COPD) in 2019: a systematic review and modelling analysis. Lancet Respir Med. 2022 May;10(5):447-458.
6. World Health Organisation (WHO).Advancing COPD care in China through a comprehensive approach. Available at: https://www.who.int/news-room/feature-stories/detail/advancing-copd-care-in-china-through-a-comprehensive-approach#:~:text=China%20has%20almost%20100%20million%20people%20living%20with,for%20more%20than%200.9%20million%20deaths%20in%202013. Last accessed February 2025
7. Yin P, et al. The Burden of COPD in China and Its Provinces: Findings From the Global Burden of Disease Study 2019. Front Public Health. 2022 Jun 3;10:859499.

8. Nucala US information available at: https://www.accessdata.fda.gov/drugsatda_docs/label/2017/125526s004lbl.pdf last accessed February 2025
9. Pavord ID, et al. Mepolizumab for Eosinophil-Associated COPD: Analysis of METREX and METREO. Int J Chron Obstruct Pulmon Dis. 2021 Jun 16;16:1755-1770.
10. The Global Strategy for Diagnosis, Management and Prevention of COPD 2024. Available at: www.goldcopd.org Last accessed: November 2024.
11. Hurst J R, et al. Susceptibility to Exacerbation in Chronic Obstructive Pulmonary Disease. *N Engl J Med*. 2010;363:1128-38.
12. 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.
13. 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(4):395-405.
14. Buchheit KM, et al. Mepolizumab targets multiple immune cells in aspirin-exacerbated respiratory disease. *J Allergy Clin Immunol*. 2021;148(2):574-584.
15. Barretto KT, et al. Human airway epithelial cells express a functional IL-5 receptor. *Allergy*. 2020;75(8):2127-2130.
16. Bajbouj K, et al. IL-5 receptor expression in lung fibroblasts: Potential role in airway remodelling in asthma. *Allergy*. 2023;78(3):882-885.
17. Siddiqui S, et al. Eosinophils and tissue remodeling: Relevance to airway disease. *J Allergy Clin Immunol*. 2023;152(4):841-857.
18. Bergantini L, et al. Regulatory T cell monitoring in severe eosinophilic asthma patients treated with mepolizumab. *Scand J Immunol*. 2021;94(1):e13031.