Stock-exchange announcement
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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 annualized rate of moderate/severe exacerbations vs. placebo with data up to two years

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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 optimized inhaled maintenance therapy. Participants were also required to have evidence of type 2 inflammation characterized 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 annualized 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 characterized 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 hospitalization. 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 program 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-center, randomized, 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 randomized to receive mepolizumab, or a placebo, as an add on to their optimized 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.

NUCALA is indicated in the U.S. for the:

- add-on maintenance treatment of adult and pediatric patients aged 6 and older with severe asthma and with an eosinophilic phenotype. NUCALA is not used to treat sudden breathing problems.

- add-on maintenance treatment of chronic rhinosinusitis with nasal polyps (CRSwNP) in adults whose disease is not controlled with nasal corticosteroids.
- 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

The following information is based on the US Prescribing Information for Nucala in licensed indications only. Please consult the full Prescribing Information for all the labelled safety information for Nucala.

CONTRAINDICATIONS
Nucala should not be administered to patients with a history of hypersensitivity to mepolizumab or excipients in the formulation.

WARNINGS AND PRECAUTIONS

- Hypersensitivity reactions (e.g., anaphylaxis, angioedema, bronchospasm, hypotension, urticaria, rash) have occurred after administration of Nucala. Discontinue Nucala in the event of a hypersensitivity reaction.
- Do not use to treat acute bronchospasm or status asthmaticus.
- Herpes zoster infections have occurred in patients receiving Nucala. Consider vaccination if medically appropriate.
- Do not discontinue systemic or inhaled corticosteroids abruptly upon initiation of therapy with Nucala. Decrease corticosteroids gradually, if appropriate.
- Treat patients with pre-existing helminth infections before therapy with Nucala. If patients become infected while receiving treatment with Nucala and do not respond to anti-helminth treatment, discontinue Nucala until parasitic infection resolves.

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥5%) in severe asthma clinical trials included headache, injection site reaction, back pain, and fatigue. Injection site reactions (e.g., pain, erythema, swelling, itching, burning sensation) occurred in 8% of subjects treated with 100 mg of Nucala versus 3% treated with placebo.

In a clinical trial in patients with EGPA receiving 300 mg of Nucala, no additional adverse reactions were identified to those reported in severe asthma clinical trials. Injection site reactions (e.g., pain, erythema, swelling) occurred in 15% of subjects treated with 300 mg of Nucala versus 13% treated with placebo.

In a clinical trial in patients with hypereosinophilic syndrome, no additional adverse reactions were identified to those reported in the severe asthma trials. Injection site reactions (e.g., burning, itching) occurred in 7% of subjects treated with 300 mg of Nucala versus 4% treated with placebo.

In a clinical trial with CRSwNP, the most common adverse reactions (incidence ≥5%) in patients receiving NUCALA 100 mg were oropharyngeal pain and arthralgia. Injection site reactions (e.g., erythema, pruritus) occurred in 2% of patients receiving NUCALA versus <1% treated with placebo.

Please see the full Prescribing Information and Patient Information for NUCALA for more information, or ask your healthcare provider.

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 hospitalization, 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.

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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 under Item 3.D "Risk factors" in GSK's Annual Report on Form 20-F for 2023, and GSK's Q2 Results for 2024.

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