GSK receives CHMP positive opinions recommending approval of Nucala (mepolizumab) in three additional eosinophil-driven diseases

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- If approved in Europe, mepolizumab would be the only treatment indicated for use in four eosinophil-driven diseases

- CHMP positive opinions advance efforts to provide the first targeted treatment for eosinophilic granulomatosis with polyangiitis (EGPA) and the first anti-IL-5 biologic treatment for patients with hypereosinophilic syndrome (HES) or chronic rhinosinusitis with nasal polyps (CRSwNP)

GlaxoSmithKline (GSK) plc today announced that the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has issued positive opinions recommending Nucala (mepolizumab), a monoclonal antibody that targets interleukin-5 (IL-5), for use in three eosinophil-driven diseases; hypereosinophilic syndrome (HES), eosinophilic granulomatosis with polyangiitis (EGPA) and chronic rhinosinusitis with nasal polyps (CRSwNP). The CHMP opinion is one of the final steps in the marketing authorisation procedure prior to approval decision by the European Commission.

The three positive opinions are based on data from pivotal studies investigating the role of targeted IL-5 inhibition with mepolizumab in these eosinophil-driven diseases. Eosinophil-driven diseases are inflammatory conditions associated with elevated levels of eosinophils, a type of white blood cell.

Christopher Corsico, Senior Vice President Development, GSK said:

> We are pleased with the CHMP's positive opinions as there are currently limited targeted treatment options available for patients in Europe with eosinophil-driven disease. If approved, mepolizumab would be the first targeted treatment available for use in four of these diseases and would further reinforce its role in targeting the underlying cause of inflammation.

HES and EGPA are both potentially life-threatening rare diseases. Inflammation in various tissues can cause a range of symptoms which are frequently severe. Standard of care for HES and EGPA often includes oral corticosteroids (OCS) and/or cytotoxic immune therapies. The availability of mepolizumab could provide patients with a new treatment option with the potential to improve clinical symptoms and reduce OCS use.

CRSwNP is a condition in which patients develop soft tissue growths called nasal polyps which can cause chronic symptoms such as nasal obstruction, loss of smell and discharge. In severe disease, patients may require repeated surgical intervention due to recurrent growths.

Mepolizumab is already approved for use in Europe as an add-on treatment for patients with severe eosinophilic asthma. Epidemiological, clinical, and pathophysiological studies strongly suggest that CRSwNP and asthma are closely linked and often coexist. Additionally, patients with EGPA frequently have severe asthma. This overlap across eosinophil-driven diseases underscores the importance of understanding the complex role of eosinophils in disease.

Mepolizumab has been studied in over 4,000 patients in a total of 41 clinical trials evaluating the role mepolizumab may play in targeting the underlying cause of inflammation and reducing eosinophils through IL-5 inhibition. Through ongoing research, GSK is committed to improving the lives of those living with disease associated with uncontrolled eosinophilic inflammation, continuously innovating in order to address the unmet needs in this broad patient group.

First approved in 2015 for severe eosinophilic asthma (SEA), mepolizumab is the first-in-class monoclonal antibody that targets IL-5. It is believed to work by preventing IL-5 from binding to its receptor on the surface of eosinophils, reducing blood eosinophils and maintaining them within normal levels. A normal level of blood

eosinophils being less than 500 eosinophils/microlitre. The mechanism of action for mepolizumab has not been definitively established.

Mepolizumab has been developed for the treatment of diseases that are driven by inflammation caused by eosinophils. It has been studied in over 4,000 patients in 41 clinical trials across a number of eosinophilic indications and has been approved under the brand name Nucala in the US, Europe and in over 25 other markets, as an add-on maintenance treatment for patients with SEA. Mepolizumab is approved in 17 markets, including Europe and the US, for paediatric use in SEA from ages 6-17 years, with approval in an additional 7 markets for use in patients with SEA aged 12-17 years. The first approval for mepolizumab in CRSwNP was granted by the FDA in July 2021. In a total of 13 markets including the US, Japan and Canada it is approved for use in adult patients with EGPA. Mepolizumab was approved for use in HES in the US in September 2020, followed by Brazil in February 2021, Argentina in May 2021 and Canada in September 2021. Mepolizumab is currently being investigated in COPD. It is not currently approved for use in COPD anywhere in the world.

About severe eosinophilic asthma

Severe asthma is defined as asthma which requires treatment with high dose inhaled corticosteroids (ICS) plus a second controller (and/or systemic corticosteroids) to prevent it from becoming ‘uncontrolled’ or which remains ‘uncontrolled’ despite this therapy. Severe asthma patients can also be categorised by long-term use of oral corticosteroids (OCS). In a sub-set of severe asthma patients, the over-production of eosinophils (a type of white blood cell) is known to cause inflammation in the lungs, this is known as severe eosinophilic asthma (SEA). Interleukin-5 (IL-5) is the main promoter of eosinophil growth, activation and survival and provides an essential signal for the movement of eosinophils from the bone marrow into the lung. Studies suggest that approximately 60% of patients with severe asthma have eosinophilic airway inflammation.

About chronic rhinosinusitis with nasal polyps (CRSwNP)

CRSwNP is a chronic inflammatory disease of the nasal passage linings or sinuses which leads to soft tissue growths known as nasal polyps and is often characterised by elevated levels of eosinophils.

The resultant swellings typically grow in both nostrils (bilateral) greatly impacting a patient due to various symptoms including nasal obstruction, loss of smell, facial pressure and nasal discharge. Surgery may be indicated for severe cases. However, polyps have a strong tendency to reoccur often leading to repeat surgery.

About hypereosinophilic syndrome (HES)

HES is a rare and under-diagnosed disorder, making it difficult to estimate its overall prevalence. Patients with HES have a persistent and marked overproduction of eosinophils, a type of white blood cell. When eosinophils infiltrate certain tissues, they can cause inflammation and organ damage which, over time, can impact patients' day-to-day ability to function. Complications can range from fever and malaise to respiratory and cardiac problems. If left untreated, the symptoms of HES become progressively worse and the disease can be life-threatening.

About eosinophilic granulomatosis with polyangiitis (EGPA)

EGPA is a chronic rare disease that is caused by inflammation in the walls of small-to-medium sized blood vessels (vasculitis). In EGPA, patients typically develop adult-onset asthma, and often allergic rhinitis and sinusitis. EGPA can result in damage to lungs, sinuses, skin, heart, gastrointestinal tract, nerves and other organs and can be life-threatening for some patients. The most common symptoms include extreme fatigue, muscle and joint pain, weight loss, sinonasal symptoms, and breathlessness.

Important safety information

The following Important Safety Information and Detailed Recommendations for Use of this product will be described in the updated summary of product characteristics (SmPC), which will be published in the revised European public assessment report EPAR), and will be available in all official European Union languages after a decision on this change to the marketing authorisation has been granted by the European Commission.

Nucala is contraindicated in patients with hypersensitivity to mepolizumab or to any of the excipients.

Nucala has not been studied in patients with organ- or life-threatening

manifestations of EGPA, or in patients with life-threatening manifestations of HES.

Nucala should not be used to treat acute asthma exacerbations.

Asthma-related adverse symptoms or exacerbations may occur during treatment. Patients should be instructed to seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment.

Abrupt discontinuation of corticosteroids after initiation of Nucala therapy is not recommended. Reduction in corticosteroid doses, if required, should be gradual and performed under the supervision of a physician.

Acute and delayed systemic reactions, including hypersensitivity reactions (e.g. anaphylaxis, urticaria, angioedema, rash, bronchospasm, hypotension), have occurred following administration of Nucala. These reactions generally occur within hours of administration, but in some instances have a delayed onset (i.e., typically within several days). These reactions may occur for the first time after a long duration of treatment.

Eosinophils may be involved in the immunological response to some helminth infections. Patients with pre-existing helminth infections should be treated for the helminth infection before starting therapy with Nucala. If patients become infected whilst receiving treatment with Nucala and do not respond to anti-helminth treatment, temporary discontinuation of therapy should be considered.

Very common (≥1/10): headache. Common (≥1/100 to

GSK’s commitment to respiratory disease

For over 50 years, GSK has led the way in developing medicines that advance the management of asthma and COPD. From introducing the world’s first selective short-acting beta agonist in 1969, to launching six treatments in five years to create today’s industry-leading respiratory portfolio, we continue to innovate so we can reach the right patients, with the right treatment. Working together with the healthcare community, we apply world-class science to discover and understand the molecules that become the medicines of tomorrow. We won’t stand still until the simple act of breathing is made easier for everyone.

GSK is a science-led global healthcare company. For further information please visit www.gsk.com/about-us.

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 Company's Annual Report on Form 20-F for 2020 and any impacts of the COVID-19 pandemic.

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