European Commission approves Nucala (mepolizumab) in three additional eosinophil-driven diseases

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For media and investors only

- Approval for the first targeted treatment for eosinophilic granulomatosis with polyangiitis and the first anti-IL-5 biologic treatment for patients with hypereosinophilic syndrome or chronic rhinosinusitis with nasal polyps in Europe

- Mepolizumab is now the only treatment approved in Europe for use in four eosinophil-driven diseases

GlaxoSmithKline (GSK) plc today announced that the European Commission has approved Nucala (mepolizumab), a monoclonal antibody that targets interleukin-5 (IL-5), for use in three additional eosinophil-driven diseases. This authorisation follows positive opinions recommended by the Committee for Medicinal Products for Human Use and authorises mepolizumab for use as an add on treatment in hypereosinophilic syndrome (HES), eosinophilic granulomatosis with polyangiitis (EGPA) and chronic rhinosinusitis with nasal polyps (CRSwNP).

Eosinophil-driven diseases are inflammatory conditions associated with elevated levels of eosinophils, a type of white blood cell. 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. HES and EGPA are both potentially life-threatening rare diseases arising from inflammation in various tissues. The inflammation can cause a range of symptoms which are frequently severe. Mepolizumab is the first approved targeted treatment for EGPA and the first anti-IL-5 biologic treatment for patients with HES or CRSwNP in Europe. These approvals make

mepolizumab the only treatment approved in Europe for use in four eosinophil-driven diseases as mepolizumab is already approved for use in Europe as an add-on treatment for patients aged six years and older with severe eosinophilic asthma (SEA).

Dr. Hal Barron, Chief Scientific Officer and President R&D, GSK, said:

> With millions of patients across Europe affected by eosinophil-driven diseases, we recognize the urgency in delivering the first approved targeted treatment for use in four of these conditions. Today's approvals reinforce the important role treatments such as mepolizumab can play in helping to improve the lives of patients with these debilitating diseases.

Individual country studies suggest that across Europe there are up to 22 million people who have CRSwNP. Patients with CRSwNP, particularly those with severe disease, may rely upon oral steroids to manage the inflammation and can require repeated surgical intervention due to recurrent growths to manage their condition. Advances in biologic therapies are providing options for these patients. Mepolizumab is now approved as an add-on therapy to intranasal corticosteroids for the treatment of adult patients with severe CRSwNP for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control.

Available data suggest that across Europe, roughly 7000 people are affected by EGPA. EGPA is characterised by widespread inflammation in the walls of small blood vessels (vasculitis). The disease may affect multiple organ systems and be associated with symptoms of fatigue, muscle and joint pain and weight loss. The burden of disease may be high with patients experiencing recurrent relapses which prevent them from carrying out everyday activities. Currently, most patients with EGPA are treated with anti-inflammatory corticosteroids or immunosuppressive medicines (i.e. medicines that reduce the activity of the immune system) which can lead to both short and long-term adverse effects. Mepolizumab is now approved as an add-on treatment for patients aged 6 years and older with relapsing-remitting or refractory EGPA.

Up to 5,000 adults in Europe are affected by HES. When eosinophils infiltrate certain tissues, they can cause inflammation which can lead to 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. The symptoms of HES may become progressively worse and can be life-threatening. HES can take many years to diagnose, and most patients continue to suffer from debilitating flares of their disease due to limited treatment options. Mepolizumab is now approved as an add-on treatment for adult patients with inadequately controlled HES without an identifiable non-haematologic secondary cause.

EGPA and HES are both rare diseases and epidemiological data is sparse, therefore the exact prevalence figures are unknown. It is probable that numbers of patients with EGPA and HES are underreported due to the rare nature of the conditions and delays in diagnosis.

Tonya Winders, CEO & President, Allergy and Asthma Network (AAN) and President of Global Allergy and Airways Patient Platform (GAAPP) commented:

> The lives of patients affected by an eosinophil-driven disease are often impacted by what can be severe or life-threatening symptoms. They may rely on both intermittent or continuous oral steroids to manage their condition or be left feeling they have no option but to endure ongoing symptoms and possible flare-ups. The availability of mepolizumab, a targeted biologic therapy, provides patients and their healthcare professionals with a new option in their armamentarium to treat hypereosinophilic syndrome, eosinophilic granulomatosis with polyangiitis, and chronic rhinosinusitis with nasal polyps.

The three approvals are based on data from pivotal trials investigating the role of targeted IL-5 inhibition with mepolizumab in these eosinophil-driven diseases. The studies demonstrated:

- In patients with HES, significantly fewer patients (15 of 54 [28%] vs 30 of 54 [56%]; P = .002) experienced a HES flare (worsening of symptoms or eosinophil threshold requiring an escalation in therapy) when treated with mepolizumab, compared to placebo, when added to standard of care treatment over the 32-week study period.

- In adult patients with EGPA, mepolizumab increased both accrued time in remission and proportion of patients achieving remission compared to placebo when added to standard of care.

- In adult patients with CRSwNP and at least one prior surgery, over 70% of whom also had a diagnosis of asthma, mepolizumab demonstrated significant improvements in both the size of nasal polyps at the end of the 52-week study and in nasal obstruction during weeks 49-52, compared to placebo when added to standard of care, as well as reducing further surgeries up to week 52.

Epidemiological, clinical, and pathophysiological studies show that CRSwNP and asthma are closely linked and often coexist. Additionally, patients with EGPA usually also have asthma which can frequently be severe. This overlap across eosinophil-driven diseases underscores the importance of understanding the complex role of eosinophils in disease.

Through ongoing research, GSK is committed to improving the lives of those living with disease associated with uncontrolled eosinophilic inflammation, continuously innovating to address the unmet needs in this broad patient group.

About Nucala (mepolizumab)

First approved in 2015 for SEA, Nucala (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. The mechanism of action for mepolizumab has not been definitively established.

Nucala is available as a solution in a prefilled pen or syringe or as a powder that comes in a vial and is made up into an injection. The patient (adults and adolescents aged 12 years and older) or caregiver can use Nucala prefilled pen or syringe themselves if their healthcare professional determines that it is appropriate, and the patient or caregiver are trained in injection techniques, whereas the vial is only for use by a healthcare professional.

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 several eosinophilic indications and has been approved in the US, the EU and in over 25 other markets, as an add-on maintenance treatment for patients with SEA. Mepolizumab is approved in 17 markets, including the EU US, for paediatric use in SEA from ages six to 17 years of age, with

approval in an additional seven 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. Mepolizumab is approved for use in patients with EGPA in a total of 14 markets including the US, Japan and Canada. Mepolizumab was first approved for use in HES in the US in September 2020 and approvals have since then been granted in an additional 5 markets. Mepolizumab is currently in clinical development for chronic obstructive pulmonary disorder (COPD) and It is not currently approved for use in COPD anywhere in the world.

Severe asthma is defined as asthma which requires treatment with high dose inhaled corticosteroids 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. 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 SEA. 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.

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.

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.

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, which will be published in the revised European public assessment report, 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

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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, GSK's Q3 Results and any impacts of the COVID-19 pandemic.

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