Stock-exchange announcement

For media and investors only

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GSK's *Nucala* (mepolizumab) approved in Japan for treatment of adults with chronic rhinosinusitis with nasal polyps

- *Nucala* is the first and only biologic in Japan with a four-weekly dosing schedule for this condition
- Chronic rhinosinusitis with nasal polyps (CRSwNP) exerts significant physical and emotional burden on patients with surgery often the only option
- This is the third indication for *Nucala* in Japan for an IL-5 mediated condition

GSK plc (LSE/NYSE: GSK) today announced that Japan's Ministry of Health, Labour and Welfare (MHLW) has approved *Nucala* (mepolizumab), a monoclonal antibody that targets interleukin-5 (IL-5), for the treatment of chronic rhinosinusitis with nasal polyps (CRSwNP) in adult patients, limited to those who are inadequately controlled with standard treatment.

Kaivan Khavandi, SVP, Global Head of Respiratory/Immunology R&D, at GSK said: "The chronic and debilitating impact that chronic rhinosinusitis with nasal polyps can have on those affected is often underestimated. This additional indication for *Nucala* in Japan could provide patients with an alternative treatment option to surgery or systemic steroids."

CRSwNP is a chronic condition that affects 1% to 4% of the general population, of whom 40% have uncontrolled disease.[1,2] People with CRSwNP experience symptoms such as nasal obstruction, loss of smell, facial pressure, sleep disturbance and nasal discharge, which can significantly affect their emotional and physical well-being.[3] In Japan, an estimated 2 million people suffer from chronic rhinosinusitis, of which about 200,000 are subject to surgery due to nasal polyps.[4]

CRSwNP is caused by chronic inflammation of the nasal lining that can cause soft tissue growth, known as nasal polyps, that develop in the sinuses and nasal cavity.[3] Over 80% of patients with CRSwNP have type 2 inflammation, which is associated with more severe disease and nasal polyp recurrence.[5-8] IL-5 is a key cytokine driving this type 2 inflammation and is present at high levels in nasal polyp tissue.[3,5-8] Although surgery can be effective at removing polyps, the underlying type 2 inflammation means they have a tendency to regrow.[7,8]

The approval is based on results of the phase III MERIT trial, which studied the efficacy and safety of mepolizumab over a 52-week period in a population of Japanese, Chinese and Russian patients with inadequately controlled CRSwNP, supported by data from the global phase III SYNAPSE study, which explored the effect of mepolizumab vs. placebo in more than 400 patients with CRSwNP.[3,9]

Mepolizumab is approved in Japan as a treatment for bronchial asthma in children aged 6 years or older and in adults with refractory asthma whose symptoms are inadequately controlled with standard treatment, and also for the treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA) inadequately responding to the standard treatment.

About the MERIT trial[9]

The phase III MERIT trial the co-primary endpoints were change from baseline in nasal obstruction visual analogue scale (VAS) score during weeks 49 to 52 compared with placebo and change in endoscopic nasal polyp score at week 52 compared with placebo.[1] Treatment with mepolizumab significantly improved nasal obstruction VAS score (mean treatment difference: -1.43 [95% CI: -2.37, -0.50]; p=0.003) and was associated with a numerical reduction in nasal polyp score at Week 52 (-0.43 [-0.89, 0.03]; p=0.067). Improvements in patient quality of life, as measured by the 22-item Sino-Nasal Outcome Test (SNOT-22) were demonstrated with mepolizumab versus placebo. Safety and tolerability data were consistent with the known profile of mepolizumab.[3,5] A similar proportion of patients experienced on-treatment adverse events in the mepolizumab (68/84 [81%]) and placebo (65/85 [76%]) groups. In

total, seven patients had treatment-related AEs (five in the placebo group and two in the mepolizumab group); none of these were SAEs.

About *Nucala* (mepolizumab)
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.[10,11] IL-5 is central to the development, maturation and activation of eosinophils, a type of white blood cell implicated in the pathogenesis of asthma and CRSwNP.[3] Evidence indicates that IL-5 has an impact on other cell types beyond eosinophils that contribute to inflammation in airways disease.[12-16] Mepolizumab binds directly to and inhibits IL-5 molecules.[10,11] Mepolizumab has been developed for the treatment of a range of IL-5 mediated diseases associated with type 2 inflammation.[10,11]

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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