Stock-exchange announcement

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Issued: 09 September 2024, London UK
EMBARGO: Sept. 9 at 14.30 BST/15.30 CEST/09.30 ET)
Embargo of SWIFT presentation @ ERS

Depemokimab late-breaking data presented at ERS show a 54% reduction in severe asthma exacerbations

- SWIFT-1 and SWIFT-2 phase III data show depemokimab delivered a statistically significant and clinically meaningful reduction in exacerbations over 52 weeks versus placebo plus standard of care, in duplicate studies
- Ultra-long-acting biologic, depemokimab, administered once every six months produced sustained suppression of a key marker of type 2 inflammation, a driver of asthma attacks and hospitalisations
- Data published simultaneously in the *New England Journal of Medicine*

GSK plc (LSE/NYSE: GSK) today presented the full results from the SWIFT-1 and SWIFT-2 phase III clinical trials which assessed the efficacy and safety of depemokimab versus placebo in adults and adolescents with severe asthma with type 2 inflammation characterised by raised blood eosinophil count.[1] The data were presented at the European Respiratory Society International Conference (7-11 September) in Vienna, Austria and simultaneously published in the *New England Journal of Medicine.*

SWIFT-1 and SWIFT-2 are duplicate studies with the same primary and secondary endpoints. Both trials met their primary endpoints with statistically significant reductions in the annualised rate of clinically significant exacerbations (asthma attacks) over 52 weeks versus placebo, with the pre-specified pooled analysis showing a significant 54% reduction in exacerbations [Rate Ratio 0.46, 95% CI, 0.36 – 0.59, p<0.001] (AER depemokimab = 0.51 exacerbations per year versus placebo = 1.11).[1]

In the pooled analysis of SWIFT-1 and SWIFT-2, there was a 72% reduction [RR 0.28, 95% CI 0.13 – 0.61, *p*=0.002] (AER: depemokimab = 0.02 versus placebo = 0.09) in the secondary endpoint of clinically significant exacerbations requiring hospitalisation or emergency department visit compared to placebo.[1] As the pooled analysis of SWIFT-1 and SWIFT-2 did not control for multiple comparisons, results with a significant p-value (<0.05) are termed nominally significant. In the individual trials, the secondary endpoints assessing quality-of-life or the symptoms-based measure, showed improvements but did not reach statistical significance versus placebo.[1]

These data are part of GSK's aspirations to advance treatment goals for those with severe asthma. Preventing exacerbations, a known risk for hospitalisation, and cause of cumulative lung damage and disease progression, has been a longstanding goal of asthma treatment and care.[2] Sustained suppression of type 2 inflammation, an underlying driver of exacerbations, could help change the course of disease.[3] Extended dosing intervals could also help tackle other barriers to optimal outcomes such as adherence or frequent healthcare appointments.[4-7]

Kaivan Khavandi, SVP, Global Head of Respiratory/Immunology R&D, said: "With a dosing schedule of just two injections per year, depemokimab has the potential to be the first approved ultra-long-acting biologic with six-month dosing. This could offer physicians and millions of patients with severe asthma an option that provides reassurance of sustained suppression of a key marker of type 2 inflammation and a reduction in the rate of exacerbations and hospitalisation – the fundamental treatment goal in asthma."

David Jackson, FRCP, MSc, PhD, lead author of SWIFT-1 and SWIFT-2, Professor of Respiratory Medicine at King's College London and Clinical Lead for Severe Asthma at Guy's and St Thomas' Hospitals, London, said: "As a physician, it is encouraging to see results of research that could evolve the management of severe asthma. For me, preventing exacerbations and particularly those that lead to hospitalisations is a treatment priority for the people I see with severe asthma. Not only are exacerbations traumatic for patients, and contribute to pressures on healthcare systems/hospitals, but each exacerbation can cause irreversible changes to the tissue of

the lungs that over time can lead to permanent loss of lung function and make a patient's breathing progressively more difficult."

Depemokimab is the first ultra-long-acting biologic to be evaluated in phase III trials; it has high binding affinity and potency for interleukin-5 (IL-5), which will enable six-month dosing intervals for patients with severe asthma.[1] IL-5 is a key cytokine (protein) in type 2 inflammation, typically detected by raised blood eosinophil count.[1] More than 80% of people with severe asthma exhibit type 2 inflammation as the underlying pathobiology of their asthma. Identification of these people could guide physicians in initiating the right treatment for the individual's type of asthma, thereby helping to reduce their risk of exacerbations.[3]

The proportion of patients experiencing any adverse event (AE) was similar between the depemokimab and placebo group in SWIFT-1 (depemokimab = 73%, placebo = 73%) and SWIFT-2 (depemokimab = 72%, placebo = 78%). No deaths or serious AEs were determined to be related to the study treatment by the investigator.[1]

The trial was conducted during a time of high COVID prevalence, and these events were recorded as the most common AE across groups.[1] There was no difference in reports of COVID between those receiving depemokimab or placebo in SWIFT-1 (depemokimab = 20%, placebo = 22%) and SWIFT-2 (15% for both depemokimab and placebo).[1] Nasopharyngitis, another name for the common cold, was the second most common AE in the pooled analysis. The proportion of patients experiencing a nasopharyngitis AE was lower in the depemokimab group than the placebo group in SWIFT-1 (depemokimab = 12%, placebo = 19%) and in SWIFT-2 (depemokimab = 13%, placebo = 21%). Safety analysis of the data continues as part of the open-label extension studies.[1]

These data will inform regulatory filings around the world. Depemokimab is currently not approved anywhere in the world.

About the depemokimab development programme
The phase III programme consists of SWIFT-1 and SWIFT-2 in severe asthma, with an open label extension study (AGILE).[1,8] SWIFT-1 and SWIFT-2 were replicate 52-week, randomised, double-blind, placebo-controlled, parallel-group, multi-centre clinical trials.[1] The trials assessed the efficacy and safety of depemokimab adjunctive therapy in 382 and 380 participants who were randomised to receive depemokimab or a placebo respectively, in addition to their standard of care treatment with medium to high-dose inhaled corticosteroids plus at least one additional controller.[1] Number of subjects included in the Full Analysis of SWIFT-1: depemokimab = 250, placebo = 132 and in SWIFT-2: depemokimab = 252, placebo = 128.[1]

The primary endpoint of reduction in the annualised rate of clinically significant exacerbations (asthma attacks) over 52 weeks vs. placebo for the individual studies were as follows:[1]

- SWIFT-1: 58% (RR 0.42 [95% CI 0.30, 0.59]; p<0.001)
  - AER = 0.46 annual exacerbation rate in the depemokimab group vs. 1.11 in the placebo group.
- SWIFT-2: 48% (RR 0.52 [95% CI 0.36, 073]; p<0.001)
  - AER = 0.56 annual exacerbation rate in the depemokimab group vs. 1.08 in the placebo group.

An additional study (NIMBLE) is underway to assess the efficacy and safety of depemokimab when participants with severe asthma are switched from mepolizumab or benralizumab.[9]

Depemokimab's half-life and high potency for IL-5 means it has the potential to provide sustained inhibition of broad inflammatory functions and is being investigated in a variety of type 2 inflammatory conditions.[1,8-13] Depemokimab is currently being evaluated in phase III trials across a range of other IL-5 mediated diseases, including OCEAN for eosinophilic granulomatosis with polyangiitis (EGPA)[10], ANCHOR 1 & 2 for chronic rhinosinusitis with nasal polyps (CRSwNP)[11,12] and DESTINY for hypereosinophilic syndrome (HES).[13]

About severe asthma and type 2 inflammation
Severe asthma is defined as asthma that requires treatment with high-dose inhaled corticosteroids plus a second controller (and/or systemic corticosteroids) or biologic therapy, to prevent it from becoming 'uncontrolled' or which remains 'uncontrolled' despite treatment.[2] Estimates suggest that severe asthma accounts for more than 60% of all asthma-related costs in some countries, with higher per-patient costs than for a patient with type 2 diabetes or a stroke.[14] Patients with severe asthma bear a significant financial burden, for medical care and lost earnings. With some exacerbations leading to sick days or hospitalisation.[14] In more than 80% of patients with severe asthma, their condition is driven by type 2 inflammation in which patients exhibit elevated levels of eosinophils (a type of

white blood cell).[3] Blood eosinophils count can be measured via a simple blood test. IL-5 is a core cytokine (protein) in type 2 inflammation alongside IL-4 and IL-13.[2] Type 2 inflammation drives the underlying pathology various immune-mediated conditions. IL-5 is responsible for the growth, activity, and survival of eosinophils.[2]

About GSK in respiratory
GSK is redefining the future of respiratory medicine as it builds on decades of pioneering work to deliver more ambitious treatment goals and develop the next-generation standard of care, 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 diseases like 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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