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THIS ANNOUNCEMENT CONTAINS INSIDE INFORMATION FOR THE PURPOSES OF THE UK VERSION OF THE MARKET ABUSE REGULATION (EU NO. 596/2014) WHICH FORMS PART OF ENGLISH LAW BY VIRTUE OF THE EUROPEAN UNION (WITHDRAWAL) ACT 2018.

IP Group plc - Portfolio company Istesso provides update on Phase 2b study of leramistat in rheumatoid arthritis

- Results reinforce leramistat's novel mechanism of action (MOA) and effectiveness in bone protection in people living with rheumatoid arthritis (RA).
- Significant improvements were seen in the key secondary endpoint of bone erosions as well as improvements in disability and fatigue in patients treated with leramistat, despite the study not meeting the primary endpoint of improvement in ACR20 versus placebo.
- Results support further evaluation of leramistat's potential to promote tissue repair in RA, as well as other chronic conditions. Istesso is sufficiently funded to conduct additional studies.

IP Group plc (LSE: IPO), which invests in breakthrough science and innovation companies with the potential to create a better future for all, is pleased to provide the following update now that Istesso Limited has provided its shareholders with the outcome of its Phase 2b study of leramistat in rheumatoid arthritis (RA).

The leramistat phase 2b study was a 12-week randomised, double-blind, placebo-controlled trial in adults with moderate-severe RA and an inadequate response to treatment with methotrexate. Although the study did not meet the primary endpoint of improvements in ACR20 versus placebo, leramistat did demonstrate statistically significant reductions in the key secondary endpoint of bone erosions, as well as improvements in disability and fatigue.[1]

Istesso highlighted that these findings demonstrate leramistat's unique mechanism of action (MOA) and support further evaluation of its potential to promote adaptive tissue repair in combination with existing disease-modifying anti-rheumatic drugs (DMARDs) in RA, as well as in other chronic conditions.

Istesso also drew attention to the fact that treatment with leramistat significantly reduced or stopped the progression of bone erosions.[1] Bone erosions are a central feature of RA and appear early in the course of the disease. Progression of bone erosions leads to bone damage and is a major driver of disability and increased mortality in people living with RA.[2,3,4,5]

Improvements in structural damage were accompanied by statistically significant benefits seen in reduced disability and fatigue for patients receiving leramistat versus placebo.[1] Fatigue in RA is widespread and its impact debilitating, affecting quality of life and is often cited as the primary cause of inability to work and job loss.[6] Current treatment options are limited and there remains a huge unmet clinical need.[6]

No new safety concerns were identified in the study. The adverse event (AE) rate was similar between groups receiving leramistat and placebo, and the majority of AEs were mild in nature and resolved without treatment.[1] No deaths were reported and no significant changes in clinical chemistry, bloods, vital signs or cardiovascular health have been noted in leramistat trials to date.[7]

Istesso will publish full study results in due course and plans further Phase 2 studies to evaluate leramistat's unique potential to promote adaptive tissue repair in RA, as well as other chronic conditions. Istesso is sufficiently funded to conduct these studies.

IP Group has an undiluted holding of 56.5% in Istesso and anticipates providing a further update on Istesso, including its valuation, in its 2024 results that will be published next month.

Greg Smith, Chief Executive Officer of IP Group, said: "We are encouraged that these results are consistent with leramistat's unique mechanism of action which supports and augments tissue repair. In addition, the impact on disability and fatigue, from which a large proportion of RA patients continue to suffer despite the widespread availability of current medications, is also highly promising. Istesso will carry out additional work to evaluate leramistat's potential to address these unmet needs and to promote adaptive tissue repair in RA and other chronic conditions, potentially in combination with existing therapies. Based on these data, we continue to believe in the market opportunity for leramistat to improve patients' health and deliver significant value for shareholders."

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Notes for editors

About IP Group

IP Group accelerates the impact of science for a better future. As the most active UK based, early stage science investor, we develop and support some of the world's most exciting businesses in deeptech, life sciences and cleantech (led by Kiko Ventures). Through Parkwalk, the UK's largest growth EIS fund manager, we also back world-changing innovation emerging in leading universities and research institutions. Our specialist investment team combines sector expertise with an international approach. Together we have a strong track record of success, having backed high-profile companies including Oxford Nanopore Technologies plc, First Light Fusion, Hysata, and Oxa. IP Group is listed on the Main Market of the London Stock Exchange under the code IPO. For more information, please visit our website at www.ipgroupplc.com.

About Istesso
Istesso is looking at chronic disease differently, focusing on repairing the damage caused by debilitating chronic conditions rather than symptom control. We stand apart, disrupting conventional thinking and seeking robust science-led treatment solutions to enable patients to live free from chronic disease. Scientists at heart, with almost 1000 years of drug discovery expertise, we are the only company to understand and exploit the body's natural biology of repair. Istesso is discovering and developing pioneering transformative medicines that enhance the body's ability to repair, redefine treatment expectations and make a lasting impact on patients' lives. To learn more please visit us at: www.istesso.co.uk

About leramistat
Leramistat is an investigational first-in-class, once-daily pill currently in phase 2 development. Its unique MOA augments the body's inherent repair response to repair and restore damaged tissue and build resilience to further damage without suppressing the immune system.[7] Leramistat has been shown to reduce the progression of structural damage and improve bone dynamics, disability and fatigue in people with RA.[7] With its good safety and tolerability profile and a low likelihood of interactions with other medicines, leramistat is ideally positioned as a potential combination therapy in RA.[7]

Leramistat offers the potential for disease resolution across a wide range of therapeutic areas including chronic diseases of auto-inflammation, autoimmunity, fibrosis or bone loss.[7] Leramistat has been granted both FDA Fast Track and Orphan Drug Designation (ODD) to support its development and expedite its review to fill an unmet medical need in idiopathic pulmonary fibrosis (IPF).

About rheumatoid arthritis
RA is a destructive chronic and debilitating autoimmune disease causing severe joint and tissue damage that can lead to disability and premature death affecting approximately 17.6 million people globally.[9,10] This figure is expected to double to ~31.7 million by 2050 and it is estimated that ~70% of those affected will be female.[12] Bone erosions appear early in the course of RA, often preceding diagnosis and up to 60% of patients have erosions within a year leading to joint damage and causing impaired function and disability.[2,4,5] Even with significant treatment advances, many patients continue to show joint deterioration and disability, and rates of RA related surgery remain relatively unchanged in many countries.[6,11]

The majority of people with RA also experience daily fatigue with significant overwhelming exhaustion affecting up to 70% of patients, and almost three quarters experiencing persistently high or worsening levels of fatigue.[6,12] Fatigue is a key contributor to increased clinical care costs, primary care consultations and employment loss, is poorly understood and managed and current treatments have a minimal effect on fatigue.[7,12]

About the study
The leramistat phase 2b study was a 12-week randomised, double-blind, placebo-controlled trial of men and women with moderate-severe RA and an inadequate response to treatment with methotrexate (MTX). The primary endpoint was efficacy of leramistat versus placebo as measured by ACR20. Secondary endpoints included assessment of structural progression and subclinical inflammation, clinical joint count composite assessments such as DAS28-CRP, ACR20/50/70 over time, patient reported outcomes and change in hsCRP.[1] The study is listed on ClinicalTrials.gov and can be accessed here: https://clinicaltrials.gov/study/NCT05460832.

RA measures used in the study
ACR20[8] is a standardised RA clinical outcome measure developed by the American College of Rheumatology to evaluate the efficacy of interventions in RA clinical trials. ACR20 response is defined as at least 20% improvement from baseline in the number of tender and swollen joints and in three of the following five criteria: patient's assessment of pain by visual analogue scale (VAS), patient's global assessment of disease activity, physician's global assessment of disease activity, patient's assessment of physical function measured by HAQ-DI and C-reactive protein (CRP).

1 Data on file - NCT05460832 (IST-06). Listed on NIH National Library of Medicine Clinical Trials register. Available at: https://clinicaltrials.gov/study/NCT05460832.
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