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News Release

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Janssen Submits Marketing Authorisation Application to the European Medicines Agency (EMA) Seeking Approval of Single Tablet Combination Therapy (STCT) of Macitentan and Tadalafil for Treatment of Patients with Pulmonary Arterial Hypertension (PAH)

This is the first and only single tablet combination therapy to be submitted for review in Europe for this rare, progressive disease

If approved, Janssen's comprehensive PAH portfolio has the potential to cover all guideline-recommended treatment pathways

BEERSE, Belgium, 26 JUNE, 2023 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced the submission of a Marketing Authorisation Application (MAA) to the European Medicines Agency (EMA) seeking approval of a single tablet combination therapy of macitentan 10 mg and tadalafil 40 mg (M/T STCT) for the long-term treatment of pulmonary arterial hypertension (PAH, World Health Organization [WHO] Group 1) in adult patients of WHO functional class (FC) II-III. The application is based on data from the Phase 3 A DUE study, which demonstrated that the M/T STCT significantly improved pulmonary haemodynamics (blood flow through pulmonary blood vessels) versus macitentan and tadalafil monotherapies in patients with PAH.[1]

PAH is a rare, progressive and life-threatening disease characterised by the constriction of small pulmonary arteries and elevated blood pressure (hypertension) in the pulmonary circulation that eventually leads to right heart failure.[2] Recently updated European Society of Cardiology/European Respiratory Society (ESC/ERS) pulmonary hypertension (PH) guidelines have strengthened recommendations on initial double combination therapy with macitentan and tadalafil for PAH patients without cardiopulmonary comorbidities.[3] Currently, this requires patients to take multiple pills as no single tablet that targets two or more PAH-specific pathways is available for these patients in Europe.

"The ESC/ERS guidelines recommend double and triple combination therapy which means that PAH patients may increasingly face more complex treatment regimens, with some taking many pills each day to manage their condition and any potential comorbidities,[3,4]" said Tamara Werner-Kiechle, M.D., EMEA Therapeutic Area Lead Neuroscience and Pulmonary Hypertension, Janssen-Cilag GmbH. "A single tablet combination could be an important new option for people living with PAH with the potential to enhance convenience and help improve adherence and outcomes.[5,6] We look forward to working with the EMA to bring this combination therapy to those in need of new options, as soon as possible."

The Phase 3 A DUE study (AC-077-A301) was designed to compare the efficacy and safety profile of M/T STCT versus macitentan and tadalafil monotherapies in patients with PAH.[1] The data were presented as a Late-Breaking Clinical Trial presentation during the American College of Cardiology's (ACC) 72nd Annual Scientific Session & Expo Together With World Heart Federation's World Congress of Cardiology, in New Orleans on 6 March 2023.[1] The study met its co-primary endpoint, demonstrating marked pulmonary haemodynamic improvement as shown by the highly statistically significant, consistent and robust pulmonary vascular resistance (PVR) reduction in participants treated with M/T STCT compared to both monotherapies at 16 weeks.[1] PVR change with M/T STCT (n=70, -45 percent

change from baseline) was significantly greater versus macitentan (n=35, -23 percent PVR change from baseline) at week 16 (treatment effect: 29 percent reduction; 95 percent confidence limit [CL]: -18 percent, -39 percent; p<0.0001).[1] PVR change with M/T STCT (n=86, -44 percent change from baseline) was also significantly greater versus tadalafil (n=44, -22 percent change from baseline) at week 16 (treatment effect: 28 percent reduction; 95 percent CL: -20 percent, -36 percent; p<0.0001).[1] Although the A DUE study was not powered to demonstrate a benefit on exercise capacity, there was a positive trend for clinically relevant improvement in 6-minute walk distance (6MWD) in favour of M/T STCT versus both monotherapies as the key secondary endpoint.[1] The safety profile of M/T STCT was consistent with the known safety profiles of the individual components, macitentan and tadalafil, and no new safety observations were made.[1] The most common adverse events were headache, oedema, anaemia, haemoglobin decrease, and hypotension. The open label arm of the A DUE study is still ongoing.[1]

"Despite advances, there remains a high unmet need for those living with PAH, a progressive disease for which there is no cure,[2]" said James F. List, M.D., Ph.D., Global Therapeutic Area Head, Janssen Research & Development, LLC. "Today's submission of the single tablet combination therapy of macitentan and tadalafil to the EMA marks a significant milestone in our ongoing commitment to transform PAH into a manageable condition and help people living with the condition lead a full life."

The application to the EMA follows a New Drug Application submitted to the U.S. Food and Drug Administration (FDA) in May 2023 seeking approval of single tablet combination therapy of macitentan and tadalafil for the treatment of patients with PAH.[7]

#ENDS#

About Pulmonary Arterial Hypertension (PAH)

PAH is a specific, rare form of pulmonary hypertension (PH) with approximately 48-55 cases per million adults, and there is currently no cure.[2,3] PAH is a serious, progressive disease with a variety of aetiologies and has a major impact on patients' functioning as well as their physical, psychological and social wellbeing.[8,9]

PAH evolves silently over years, as symptoms such as breathlessness, dizziness and fatigue are non-specific and can be confused with more common conditions like asthma and chronic obstructive pulmonary disease (COPD).[2] On average it takes two years from the onset of symptoms for PAH to be diagnosed, and in some instances up to four years.[2,10] This means that by the time a patient is diagnosed, their PAH is typically in an advanced stage with severe symptoms and a poor prognosis.[2] The last decade has seen significant advances in the understanding of the pathophysiology of PAH, transforming the prognosis for PAH patients from symptomatic improvements in exercise tolerance 10 years ago, to delayed disease progression today.[3] However, PAH patients are facing a greater pill burden due to complex treatment regimens involving multiple pills.[4,11] The PAH patient population is also ageing, leading to an increasing number of concomitant medications to treat comorbidities.[3]

About macitentan/tadalafil STCT

Macitentan 10 mg and tadalafil 40 mg STCT is a therapy that combines the ERA, macitentan, and the PDE5i, tadalafil.

About OPSUMIT® (macitentan)

OPSUMIT®, as monotherapy or in combination, is indicated for the long-term treatment of PAH in adult patients of WHO Functional Class (FC) II to III.

Efficacy has been shown in a PAH population including idiopathic and heritable PAH, PAH associated with connective tissue disorders, and PAH associated with corrected

simple congenital heart disease. The use of OPSUMIT® in patients with PAH (WHO Group I), a type of PH, was demonstrated in the pivotal SERAPHIN trial, the largest (n=742) long-term (average treatment duration=2 years) outcomes-based trial of an ERA in PAH.[12]

For further information on macitentan, please see the Summary of Product Characteristics at: https://www.ema.europa.eu/en/documents/product-information/opsumit-epar-product-information_en.pdf

About tadalafil

Tadalafil is indicated in adults for the treatment of PAH, classified as WHO functional class II and III, to improve exercise capacity. Efficacy has been shown in idiopathic PAH (IPAH) and in PAH related to collagen vascular disease.[13]

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity, and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular, Metabolism & Retina; Immunology; Infectious Diseases & Vaccines; Neuroscience; Oncology; and Pulmonary Hypertension.

Learn more at www.janssen.com/emea. Follow us at www.twitter.com/janssenEMEA for our latest news. Janssen Pharmaceutica NV, Janssen-Cilag GmbH, and Janssen Research & Development, LLC are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding product development and the potential benefits and treatment impact of macitentan/tadalafil STCT. The reader is

cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialise, actual results could vary materially from the expectations and projections of Janssen Pharmaceutica NV, Janssen-Cilag GmbH, Janssen Research & Development, LLC, any of the other Janssen Pharmaceutical Companies and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; competition, including technological advances, new products and patents attained by competitors; challenges to patents; changes in behavior and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended January 1, 2023, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Quarterly Reports on Form 10-Q and other filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov*,* www.jnj.com *or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.*

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