FOR EMEA AND UK MEDICAL AND TRADE MEDIA

News Release

Media Contact:
Zayn Qureshi
Phone: +44 7760 334666
zqureshi@its.jnj.com

Investor Contact:
Raychel Kruper
Phone: +1 732-524-6164
RKruper@its.jnj.com

Late-Breaking Phase 3 A DUE Data Show Investigational Single-Tablet Combination Therapy of Macitentan and Tadalafil Significantly Improves Pulmonary Haemodynamics versus Monotherapy in Patients with Pulmonary Arterial Hypertension (PAH)

Study findings presented during the American College of Cardiology's 72nd Annual Scientific Session & Expo Together With World Heart Federation's World Congress of Cardiology

European Society of Cardiology/European Respiratory Society (ESC/ERS) PH guidelines recommend initial dual combination therapy with macitentan and tadalafil for PAH patients without cardiopulmonary comorbidities[1]

BEERSE, Belgium, 6 March, 2023 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced results from the Phase 3 A DUE study (NCT03904693), which showed an investigational once-daily, single-tablet combination therapy, also known as fixed-dose combination, of macitentan 10 mg and tadalafil 40 mg (M/T STCT), significantly improved pulmonary haemodynamics (blood flow through pulmonary blood vessels) versus macitentan and tadalafil monotherapies in pulmonary arterial hypertension (PAH) patients with World Health Organization (WHO) functional class (FC) II or III.[2] The data were presented today as a Late-Breaking Clinical Trial presentation during the American College of Cardiology's 72nd Annual Scientific Session & Expo Together With World Heart Federation's World Congress of Cardiology.

EM-124643
March 2023

PAH is a rare, progressive and life-threatening blood vessel disorder characterised by the constriction of small pulmonary arteries and elevated blood pressure in the pulmonary circulation that eventually leads to right heart failure.[3] Recently updated European Society of Cardiology/European Respiratory Society (ESC/ERS) PH guidelines have strengthened recommendations on initial dual combination therapy with macitentan and tadalafil for PAH patients without cardiopulmonary comorbidities.[1] Currently, this requires patients to take multiple pills as no single tablet that combines two or more PAH-specific pathways is available for these patients.

"Targeting different pathways in the treatment of PAH has demonstrated clear clinical benefits, yet current treatment regimens are cumbersome and create a significant pill burden for patients, many of whom take a large number of pills each day to treat their PAH and various comorbidities," said Kelly Chin, M.D., Professor of Internal Medicine and Director of the Pulmonary Hypertension Program at UT Southwestern Medical Center, and an investigator in the A DUE study.[4,5,6*] "The results from this study demonstrate that a single-tablet combination has the potential to support initial dual combination therapy and rapid escalation from monotherapy, which may improve functional outcomes and help close the gap from guideline recommendations to clinical practice.[2]"

The A DUE study is a double-blind, randomised, active-controlled, multi-centre, adaptive parallel-group study designed to compare the efficacy and safety of investigational M/T STCT versus macitentan and tadalafil monotherapies in patients with PAH.[7] A total of 187 adult PAH patients from across 148 sites in 19 countries worldwide in WHO FC II or III who were treatment naïve or on a stable dose of an endothelin receptor antagonist (ERA) or a phosphodiesterase type 5 inhibitor (PDE5i) for at least three months, were enrolled in the study.[7] The primary endpoint is pulmonary vascular resistance (PVR) measured 16 weeks following initiation of treatment expressed as the ratio of geometric means to baseline.[7]

Secondary efficacy outcome measures included change from baseline in exercise capacity as measured by change in 6-minute walk distance (6MWD) at the end of double-blind treatment at week 16 compared to baseline.[7]

Following the double-blind treatment period, patients transitioned to the open-label treatment period for 24 months. Baseline characteristics were balanced across treatment arms except for a higher proportion of WHO FC II patients in the M/T STCT arm and a greater time from diagnosis of PAH in the macitentan arm.[7]

"The guiding light of our PH research is the goal of transforming PAH into a manageable condition, so we're constantly looking for ways to improve both clinical outcomes and the treatment experience," said James List, M.D., Ph.D., Global Therapeutic Area Head, Cardiovascular, Metabolism, Retina & Pulmonary Hypertension, Janssen Research & Development, LLC. "A single-tablet combination has the potential to be an important new option for helping physicians optimise disease management with the potential to enhance convenience and help improve adherence and outcomes.[8]"

Key A DUE Study Findings

The A DUE study met its co-primary endpoint, demonstrating marked pulmonary haemodynamic improvement as shown by the highly statistically significant, consistent and robust PVR reduction in participants treated with M/T STCT compared to both monotherapies.[2] PVR change with M/T STCT (n=70) was significantly greater versus macitentan (n=35, treatment effect: 29 percent; 95 percent confidence limit [CL]: -18 percent, -39 percent; $p<0.0001$). PVR change with M/T STCT (n=86) was also significantly greater versus tadalafil (n=44, treatment effect: 28 percent; 95 percent CL: -20 percent, -36 percent; $p<0.0001$).[2]

Although the A DUE study was not powered to demonstrate a benefit on exercise capacity, there was a clinically relevant improvement in 6MWD.

- At week 16, treatment effect was not statistically significant; however a clinically relevant improvement in 6MWD in favour of M/T STCT versus monotherapies was observed. Adjusted treatment effect in 6MWD, change from baseline, in the M/T STCT (n=70) versus macitentan group (n=35) was 16.04m (CL: -17.0, 49.08; p=0.380) and 25.37m in the M/T STCT (n=86) versus tadalafil group (n=44, CL: -0.93, 51.59; p =0.059).[2]
- The safety profile of M/T STCT was consistent with the known safety profiles of macitentan and tadalafil monotherapies and no new safety observations were made.[2]

#ENDS#

**Dr. Chin received payment for her participation in the A DUE study.*

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.[1,3] 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.[9,10]

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).[3] On average it takes two years from the onset of symptoms for PAH to be diagnosed, and in some instances up to four years.[3,11] 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.[3] However, 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]

FOR EMEA AND UK MEDICAL AND TRADE MEDIA

About macitentan/tadalafil STCT

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

About OPSUMIT® (macitentan)

OPSUMIT® is indicated for the long-term treatment of PAH (WHO Group I) to reduce the risks of disease progression and hospitalisation for PAH. 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 (WHO Group 1 PH), 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, and

FOR EMEA AND UK MEDICAL AND TRADE MEDIA

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 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.*

###

[1] 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Heart J.* 2022; 43, 3618–3731. https://doi.org/10.1093/eurheartj/ehac237.
[2] Chin K, Jansa P, Fan F, et al. Efficacy and safety of macitentan tadalafil fixed dose combination in pulmonary arterial hypertension: results from the randomized controlled phase III A DUE study. Oral presentation at American College of Cardiology (ACC) Scientific Sessions, 4-6 March 2023.
[3] Vachiéry JL, Gaine S. Challenges in the diagnosis and treatment of pulmonary arterial hypertension. *Eur Respir Rev.* 2012; 21:313-20.

EM-124643
March 2023

[4] Grady D, et al. Medication and patient factors associated with adherence to pulmonary hypertension targeted therapies. *Pulm Circ* 2018; 8:1–9.
[5] Lauffenburger JC, et al. Effect of combination therapy of adherence among US patients initiating therapy for hypertension: a cohort study. *J Gen Intern Med* 2017; 32(6):619–25.
[6] Grill S, Bruderer S, Sidharta PN, et al. Bioequivalence of macitentan and tadalafil given as fixed-dose combination or single-component tablets in healthy subjects. *Br J Clin Pharmacol*. 2020;86(12):2424-2434.
[7] Clinicaltrials.gov. Clinical Study to Compare the Efficacy and Safety of Macitentan and Tadalafil Monotherapies With the Corresponding Fixed-dose Combination Therapy in Subjects With Pulmonary Arterial Hypertension (PAH) (A DUE). Available at: https://www.clinicaltrials.gov/ct2/show/NCT03904693 Last accessed: February 2023
[8] Shao L, Chan P, Tomlinson B, et al. Single-pill combinations for hypertension: first line treatment for all? *Curr Med Res Opin.* 2018;35(1):113-115.
[9] Hoeper MM, Gibbs JS. The changing landscape of pulmonary arterial hypertension and implications for patient care. *Eur Respir Rev*. 2014;23:450-457.
[10] Chin KM, Maitland MG, Channick RN, et al. Psychometric validation of the Pulmonary Arterial Hypertension-Symptoms and Impact (PAH-SYMPACT) questionnaire: results of the SYMPHONY trial. *Chest*. 2018;154:848-861.
[11] Armstrong I, Billings C, Kiely DG, et al. The patient experience of pulmonary hypertension: a large cross sectional study of UK patients. *BMC Pulm Med*. 2019;19:67.
[12] Opsumit Summary of Product Characteristics. Available at https://www.ema.europa.eu/en/documents/product-information/opsumit-epar-product-information_en.pdf Last accessed February 2023.
[13] Adcirca Summary of Product Characteristics. Available at https://www.ema.europa.eu/en/documents/product-information/adcirca-epar-product-information_en.pdf Last accessed February 2023.