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News Release

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New Data Demonstrate the Benefits of Early Use of UPTRAVI® (selexipag) in Delaying Disease Progression in a Broad Population of Patients with Pulmonary Arterial Hypertension (PAH)

Post-hoc pooled data analysis of PAH patients suggests that targeting the prostacyclin pathway with selexipag within a short timeframe after diagnosis may reduce the risk of disease progression[1,2]

PAH is a rare, progressive, and life-threatening condition with no cure; preventing disease progression is a key treatment goal[3,4,5]

ALLSCHWIL, Switzerland, 30 August 2021 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced results from a post-hoc pooled analysis of the Phase 3 GRIPHON and Phase 3b TRITON clinical trials evaluating the impact of early initiation of UPTRAVI® (selexipag) on disease progression, in a large population of PAH patients.

Featured as an oral presentation at ESC Congress 2021 (organized by the European Society of Cardiology), results from a post-hoc pooled data analysis of PAH patients treated with selexipag within 6 months of diagnosis in the Phase 3 GRIPHON and Phase 3b TRITON clinical trials showed that early initiation of selexipag reduced the risk of disease progression (first event) by 52 percent compared with the control group (hazard ratio [HR] 0.48; 95 percent confidence interval [CI] 0.35, 0.66; n = 649).[1,2]

"PAH is a rare, progressive and life-threatening condition for which there is no cure. Preventing disease progression and maintaining low-risk status for PAH patients is therefore vitally important, and proactive treatment planning is essential to effectively utilize available therapies," said Dr. Gerry Coghlan, Consultant Cardiologist at The Royal Free Hospital, London, UK.[*] "The GRIPHON and TRITON pooled analysis results support the principle of earlier treatment escalation with therapies targeting the prostacyclin pathway, such as selexipag, if we are to prevent disease progression events and improve long-term patient outcomes."

Due to the rare nature of the condition, people living with PAH are typically diagnosed in an advanced stage with severe symptoms and a poor prognosis.[3] The overall treatment goal for people living with PAH is achieving or maintaining a low-risk status.[4] Combination therapy (using two or more classes of drugs simultaneously) is recommended in clinical guidelines, based on a strong body of evidence, to help improve symptoms and function early, and prevent disease progression events.[4,6]

The GRIPHON and TRITON pooled analysis involved patients who had been diagnosed with PAH within six months of randomization (n = 649; 404 from GRIPHON and 245 from TRITON). A comparison was made between those on active therapy with selexipag (n = 329) and those on control therapy with placebo (n = 320).[1,2] Disease progression endpoints were as defined in the GRIPHON and TRITON studies:[2] time from randomization to the first morbidity event or death (all causes) up to seven days after the last study drug intake.[7,8,9] Selexipag or placebo (control) were given as part of triple therapy (with an endothelin receptor antagonist [ERA] and phosphodiesterase 5 inhibitor [PDE5i]) in 44 percent, double therapy (with an ERA or PDE5i) in 32 percent and as monotherapy in 24 percent of patients.[†1,2]

Selexipag reduced the risk of disease progression (first event) by 52 percent compared with the control group (HR 0.48 [95 percent CI 0.35, 0.66]; n = 649). There were 67 patients (20 percent) in the selexipag group and 116 patients (36 percent) in the control group who experienced a disease progression event.[1,2]

Among patients who received selexipag on top of double therapy (triple therapy group), risk of disease progression was reduced by 48 percent compared with the double therapy control group (n = 285; 145 in the selexipag group and 140 in the placebo control group; HR: 0.52 [95 percent CI 0.30, 0.92]).[2]

"At Janssen, we are committed to advancing scientific and clinical knowledge to enhance approaches to PAH treatment and care. This analysis reinforces the role of selexipag in early treatment escalation to help reduce the risk of disease progression and improve long-term outcomes for people living with PAH," said Alessandro Maresta, M.D., Vice President and Head of Medical Affairs, Pulmonary Hypertension Therapeutic Area, Janssen.[‡] "We will continue to invest in science, research and collaboration with the medical community, as we work towards our ambition of transforming PAH into a long-term, manageable condition."

Adverse events (AEs) reported in the GRIPHON and TRITON clinical trials were consistent with the known safety profiles of the studies' medications.[7,8]

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*Dr Coghlan has provided paid consultancy services for Janssen in relation to research and advisory boards. He has not been compensated for any media work.

†HRs and 95 percent CI for time to first disease progression event up to end of double-blind treatment (selexipag/placebo) plus seven days were estimated using a Cox regression model which included treatment as a factor, and baseline prognostic factors and study as covariates.[2]

‡Alessandro Maresta is an employee of Actelion Pharmaceuticals Ltd, a Janssen Pharmaceutical Company of Johnson & Johnson.

About Pulmonary Arterial Hypertension (PAH)
PAH (World Health Organization [WHO] Group 1 Pulmonary Hypertension [PH]) is a specific and rare form of PH affecting approximately 15–60 people per million in Europe, for which there is no cure.[3,4] PAH is caused when the walls of the pulmonary arteries (blood vessels leading from the right side of the heart to the lungs) become thick and stiff, narrowing the space for blood to flow and causing an increase in blood pressure to develop in the lungs, which can ultimately lead to right heart failure and death.[10,11] PAH is a serious, progressive disease with a variety of etiologies and has a major impact on patients' functioning as well as their physical, psychological and social wellbeing.[5,12] 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.[3,13] 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]

About Selexipag
Selexipag is a selective prostacyclin IP receptor agonist approved in the European Union (EU) by the European Medicines Agency (EMA) for the long-term oral treatment of PAH in adult patients with WHO functional class (FC) II–III, either as combination therapy in patients insufficiently controlled with ERA and/or a PDE5i, or as monotherapy in patients who are not candidates for these therapies.[14] Selexipag, originally discovered and synthesized by Nippon Shinyaku, is the only globally-available oral treatment that works on the prostacyclin pathway with evidence of long-term outcomes.[15] It is licensed for the oral treatment of PAH in more than 60 countries. Selexipag has also been approved by the U.S. Food and Drug

Administration (FDA) for intravenous (IV) treatment of PAH in adult patients with WHO FC II–III, who are temporarily unable to take oral therapy.[16]

The most common AEs include headache, diarrhea, nausea, jaw pain, myalgia, pain in extremities, vomiting, flushing and arthralgia.[14]

Important Safety Information
For complete prescribing information, please visit:
https://www.ema.europa.eu/en/documents/product-information/uptravi-epar-product-information_en.pdf

About GRIPHON
GRIPHON (Prostacyclin [P**G**I2] **R**eceptor agonist **I**n **P**ulmonary arterial **H**ypertensi**ON**), (2009-014490-41) is the largest randomized, controlled clinical trial ever conducted in PAH patients. This double-blind, multicenter study evaluated the long-term efficacy and safety of oral selexipag and included almost 400 patients who were already receiving double combination PAH treatment. The study provided the first randomized, controlled evidence for triple oral combination therapy in PAH. Selexipag was shown to delay disease progression and significantly reduce the risk of hospitalization compared with placebo, as well as improving exercise capacity. Overall, the most common AEs in the selexipag group were consistent with the known side effects of prostacyclin, including headache, diarrhea, nausea, and jaw pain.[7]

In the GRIPHON clinical trial, a morbidity event, confirmed by the Critical Event Committee (CEC), was defined as any of the following: hospitalization for worsening of PAH; worsening of PAH resulting in need for lung transplantation or balloon atrial septostomy; initiation of parenteral prostanoid therapy or chronic oxygen therapy due to worsening of PAH; disease progression which was defined by a decrease in 6-minute walk distance (6MWD) from baseline (≥15 percent, confirmed by a second test on a different day) combined with worsening of WHO FC for patients belonging to WHO FC II/III at baseline, or combined with the need for additional PAH-specific therapy for patients belonging to WHO FC III/IV at baseline.[7]

About TRITON
TRITON (2015-003438-28) is a multicenter, double-blind, placebo-controlled, Phase 3b study, that randomized 1:1 newly diagnosed, treatment-naïve, PAH patients to initial triple oral or initial double oral combination therapy. In the TRITON clinical trial, both the initial triple oral therapy and initial double oral therapy arms demonstrated reductions in the primary endpoint, pulmonary vascular resistance at week 26, with no statistical difference observed between both groups. However, a signal of reduced risk of disease progression was observed in the initial triple oral combination therapy group compared to the initial double oral therapy group (exploratory analysis), highlighting a need for further evaluation of disease progression endpoints. Secondary endpoints, tested hierarchically, included change in 6MWD and N-terminal pro B-type natriuretic peptide (NT-proBNP) at week 26, time to disease progression (centrally adjudicated) from randomization until the end of observation period plus seven days, and absence of worsening WHO FC at

week 26. Safety was reported up to end of the observation period. The trial enrolled 247 patients.[8]

In the TRITON clinical trial, disease progression, as adjudicated by the CEC, was defined as any of the following: death; hospitalization for worsening PAH; initiation of prostacyclin, a prostacyclin analogue, or a prostacyclin receptor agonist for worsening PAH; clinical worsening defined as a post-baseline decrease in 6MWD by >15 percent from the highest 6MWD obtained at or after baseline, accompanied by WHO FC III or IV symptoms (both conditions confirmed at two consecutive post-baseline visits separated by 1–21 days).[8,9]

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, Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology, and Pulmonary Hypertension. Learn more at https://www.janssen.com/emea/. Follow us at https://twitter.com/janssenemea.

Janssen-Cilag International NV, is the marketing authorization holder for UPTRAVI® (selexipag) in the EU. Janssen-Cilag International NV and Actelion Pharmaceuticals Ltd, are two 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 UPTRAVI® (selexipag). 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 materialize, actual results could vary materially from the expectations and projections of Actelion Pharmaceuticals Ltd, Janssen-Cilag International NV and/or 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; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; 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 3, 2021, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in

the company's most recently filed Quarterly Report on Form 10-Q, and the company's subsequent 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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