News Release

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Results from Expert Delphi Consensus Survey on Treatment of Pulmonary Arterial Hypertension (PAH) with Oral Prostacyclin Pathway Agents (PPAs) Published in *CHEST* Journal

Panel of 19 Physicians Provided Consensus Opinions on Clinical Scenarios in Which They Considered Adding Oral PPAs in Patients with PAH on ERA + PDE-5 Inhibitor Background Therapy

SOUTH SAN FRANCISCO, CA, April 3, 2020 – Actelion Pharmaceuticals US, Inc., a Janssen Pharmaceutical Company of Johnson & Johnson, today announced that *CHEST,* the official publication of the American College of Chest Physicians, published results from an expert Delphi consensus survey that help provide additional insights for physicians to advance the care of patients with pulmonary arterial hypertension (PAH).

The Prostacyclin International Expert Panel developed the consensus opinions based on common clinical scenarios in which they considered adding oral prostacyclin pathway agents (PPAs), including UPTRAVI® (selexipag), in WHO functional class (FC) II and III PAH patients on endothelin receptor antagonist (ERA) and phosphodiesterase type 5 (PDE-5) inhibitor background therapy.

The consensus opinions were formed utilizing the RAND/University of California Los Angeles Appropriateness Method, which incorporates the Delphi method and nominal group technique. Consensus was reached on when they considered adding UPTRAVI for 13 clinical scenarios in PAH patients (WHO FC II and III) with either idiopathic, heritable, and drug- or toxin-induced PAH (IPAH+) or connective tissue disease-associated PAH (PAH-CTD) on ERA and PDE-5 inhibitor background therapy. The panel considered parenteral prostacyclin therapy the treatment of choice in IPAH+ and PAH-CTD patients with high-risk hemodynamics irrespective of other clinical factors.[1] The results are not intended to be formal treatment guidelines and cannot replace assessment and/or clinical decision-making by a qualified healthcare practitioner for an individual patient.

"The current gaps in information about the use of oral PPAs in patients with FC II or III symptoms combined with a dual ERA and PDE-5 inhibitor background therapy create ambiguity in prescribing practices and in managing these patients," said lead study author Vallerie McLaughlin*, MD, FCCP, University of Michigan, Ann Arbor. "While each patient faces a unique set of circumstances and struggles, we hope these consensus opinions provide a perspective into clinical scenarios when adding an oral prostacyclin pathway agent in those patients currently receiving an ERA and PDE-5 inhibitor as background therapy may be appropriate."

"Actelion is committed to helping healthcare providers improve outcomes for patients through greater understanding and management of PAH," said Siân Walker, MD, Vice President and Head of Medical Affairs at Actelion Pharmaceuticals US, Inc. "We are proud to support the meaningful work being done by these frontline physicians who have been dedicated to advancing research, education and care of this progressive disease."

** Dr. McLaughlin has received research support from Actelion and has served as a paid consultant to the company.*

ABOUT THE PROSTACYCLIN INTERNATIONAL EXPERT PANEL CONSENSUS OPINIONS

The Prostacyclin International Expert Panel was convened to develop consensus opinions on selected common clinical scenarios considered when adding an oral PPA (UPTRAVI and oral treprostinil) to WHO FC II and III PAH patients on an ERA and PDE-5 inhibitor background therapy. Panelists ranked clinical factors that they typically use to make routine treatment decisions regarding the initiation of oral PPAs with the following considered in order of importance (within each FC): hemodynamics (based on thresholds defined by the 2015 European Society of Cardiology and European Respiratory Society guidelines[2]), PAH-associated hospitalization within the prior six months, right ventricular function, BNP/NT-pro-BNP levels, and 6-minute walk distance. These factors were then used to develop clinical scenarios about patients with either IPAH+ or PAH-CTD who were on an ERA and PDE-5 inhibitor with FC II or FC III symptoms. The panelists evaluated the clinical scenarios by completing two rounds of Delphi surveys and utilizing the nominal group technique during a face-to-face meeting, which resulted in a total of 14 consensus opinions. Thirteen of those consensus opinions were for clinical scenarios in which the addition of UPTRAVI was considered to ERA and PDE-5 inhibitor background therapy, and there was one consensus opinion in which parenteral prostacyclin therapy was considered treatment of choice for IPAH+ and PAH-CTD patients with high-risk hemodynamics irrespective of other clinical factors.[1]

The Prostacyclin International Expert Panel was not a consensus conference such as one held by a task force convened for the purpose of developing treatment guidelines. The Prostacyclin International Expert Panel opinion survey statements are not intended to be formal treatment guidelines or recommendations, and survey results presented here must be validated with rigorous prospective studies. The Prostacyclin International Expert Panel opinion survey statements <u>cannot</u> replace assessment and/or clinical decision-making by a qualified healthcare practitioner for an individual patient. These statements do not address all

possible clinical situations, nor do these statements account for additional individual patient factors not specifically stated.[1]

Funding for the Prostacyclin International Expert Panel was provided by Actelion to support the use of independent providers of Delphi methodology expertise and nominal group technique, survey creation, data analysis, medical communication, and meeting management. Actelion played no role in the literature search and analysis, development of surveys used to gather consensus, or data analysis. No Actelion employees were present at the face-to-face meeting during which consensus statements were finalized. The current manuscript was drafted, critically reviewed, and edited solely by the authors with support from an independent professional medical communications agency. Actelion reviewed the final manuscript only to ensure accuracy of UPTRAVI background information; no edits were made to the manuscript based on this review.

ABOUT PULMONARY ARTERIAL HYPERTENSION (PAH)

PAH is a specific form of PH that causes the walls of the pulmonary arteries (blood vessels leading from the right side of the heart to the lungs) to become thick and stiff, narrowing the space for blood to flow, and causing an increased blood pressure to develop within the lungs. 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. There is currently no cure for PH and it is often fatal.[2,3,4] 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.

ABOUT UPTRAVI® (selexipag)

UPTRAVI is an oral selective prostacyclin IP receptor agonist for the treatment of PAH and is the only treatment that works on the prostacyclin pathway indicated to delay disease progression and reduce the risk of PAH related hospitalizations. UPTRAVI is the only oral treatment that works on the prostacyclin pathway with

evidence of long-term outcomes. UPTRAVI is available for the treatment of PAH in more than 40 countries. In the US, UPTRAVI is indicated for the treatment of PAH to delay disease progression and reduce the risk of hospitalization. In Europe, UPTRAVI is indicated for the long-term treatment of PAH in adult patients with WHO FC II–III, either as combination therapy in patients insufficiently controlled with an ERA and/or a PDE-5 inhibitor, or as monotherapy in patients who are not candidates for these therapies.[5]

What is UPTRAVI?

UPTRAVI® (selexipag) is a prescription medicine used to treat pulmonary arterial hypertension (PAH, WHO Group 1), which is high blood pressure in the arteries of your lungs.

UPTRAVI can help slow down the progression of your disease and lower your risk of being hospitalized for PAH.

It is not known if UPTRAVI is safe and effective in children.

What is the most important information about UPTRAVI?

Who should not take UPTRAVI?

- Do not take UPTRAVI if you take gemfibrozil because this medicine may affect how UPTRAVI works and cause side effects

What should I tell my doctor before taking UPTRAVI?

Tell your doctor if you:

- Have liver problems
- Have narrowing of the pulmonary veins (veins in your lungs). This is called pulmonary veno-occlusive disease (PVOD)
- Are pregnant or plan to become pregnant. It is not known if UPTRAVI will harm your unborn baby

- Are breastfeeding or plan to breastfeed. It is not known if UPTRAVI passes into your breast milk. You and your doctor should decide if you will take UPTRAVI or breastfeed. You should not do both
- Have any other medical conditions
- Are taking any other prescription or over-the-counter medicines, vitamins, or herbal supplements

What are the possible side effects of UPTRAVI?

The most common side effects are:

- Headache
- Nausea
- Pain in arms or legs
- Low red blood cell count
- Diarrhea
- Muscle pain
- Temporary reddening of the skin (flushing)
- Less appetite than usual
- Jaw pain
- Vomiting
- Joint pain
- Rash

Talk to your doctor if you have a side effect that bothers you or does not go away. These are not all the possible side effects of UPTRAVI. For more information, ask your doctor or pharmacist.

You may report side effects to **FDA at 1-800-FDA-1088** or **www.fda.gov/medwatch**.

Keep UPTRAVI and all medicines out of the reach of children.

What other medicines might interact with UPTRAVI?

- UPTRAVI and other medicines may affect each other, causing side effects. Tell your doctor about all the medicines you are taking. Do not start any new medicine until you check with your doctor

How should I take UPTRAVI?

- Take UPTRAVI exactly as your doctor tells you to take it. Usually, your doctor will have you take UPTRAVI twice a day. Taking UPTRAVI with food may help you tolerate UPTRAVI better
- Swallow UPTRAVI tablets whole. Do not split, crush, or chew tablets
- Tell your doctor if you have any form of liver disease. Your doctor may need to change your dose of UPTRAVI
- UPTRAVI is measured in micrograms (mcg). Tablets come in the following strengths: 200, 400, 600, 800, 1000, 1200, 1400, and 1600 mcg

Please see full **Prescribing Information** and **Patient Product Information**.

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 www.janssen.com. Follow us at www.twitter.com/JanssenGlobal. Actelion Pharmaceuticals US, Inc. is one 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 UPTRAVI® (selexipag) and the Results of an Expert Consensus Survey on the Treatment of Pulmonary Arterial Hypertension. 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 US, Inc., 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 December 29, 2019, 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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References

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