News Release

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UPTRAVI® (selexipag) Receives FDA Approval for Intravenous Use in Adult Patients with Pulmonary Arterial Hypertension (PAH)

New formulation allows for uninterrupted treatment for PAH patients temporarily unable to take oral therapy

TITUSVILLE, N.J. – July 30, 2021 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today that the U.S. Food and Drug Administration (FDA) has approved UPTRAVI® (selexipag) injection for intravenous (IV) use for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) in adult patients with WHO functional class (FC) II–III, who are temporarily unable to take oral therapy. UPTRAVI® IV is a therapeutic option that will allow patients to avoid short-term treatment interruptions and stay on UPTRAVI® therapy, as uninterrupted treatment is considered key for individuals with PAH. UPTRAVI® tablets were first approved by the FDA in 2015 to delay disease progression and reduce the risk of hospitalization for PAH.[1]

"Given the progressive nature of this disease, maintaining treatment is important to help control PAH. However, there are times where patients may be unable to take oral medications. For patients on UPTRAVI, bridging short-term temporary interruptions of UPTRAVI tablets with UPTRAVI IV may maintain the treatment effect and avoid the need to change therapy or re-titrate UPTRAVI tablets after re-initiation," said Kelly Chin, M.D.*, UPTRAVI® IV study senior author and Associate Professor of Internal Medicine and Director of the Pulmonary Hypertension Program at The University of Texas Southwestern Medical Center.

The FDA approval of the New Drug Application (NDA) for UPTRAVI® is based upon the findings from a prospective, multi-center, open-label single sequence cross-over Phase 3 study designed to assess the safety, tolerability and pharmacokinetics of temporarily switching between UPTRAVI® tablets and UPTRAVI® IV. The results of the study were

published earlier this year in *Respiratory Research* and examined switching from a stable dose of UPTRAVI® tablets to a corresponding dose of UPTRAVI® IV and back to UPTRAVI® tablets.[2]

"Today marks an important day for patients who rely on UPTRAVI, as this new intravenous formulation meets a current unmet need for these patients. As part of our commitment to investing in research and understanding the science around the potential of UPTRAVI, we're inspired by this approval and are proud to be paving the way to advance treatment options and care for patients with PAH," said Neil Davie, PhD**, Global Therapeutic Area Head, Pulmonary Hypertension, Janssen.

The UPTRAVI® IV study enrolled 20 patients who received all UPTRAVI® doses (either tablets or IV). The study found that the switch between UPTRAVI® tablets and UPTRAVI® IV was well tolerated with no unexpected safety findings. Adverse events (AEs) that resulted from UPTRAVI® IV were similar to those associated with UPTRAVI® tablets, with the exception of infusion site reactions reported in two patients (both of which were considered mild-to-moderate in intensity and neither led to study and/or treatment discontinuation). The prostacyclin-associated AEs included headache, diarrhea, nausea, vomiting, pain in jaw, myalgia, pain in extremity, flushing, and arthralgia.[2]

*Kelly Chin, M.D., has received research support from Janssen and has served as a paid consultant to the company. She has not been compensated for any media work.
**Neil Davie is an employee of Actelion Pharmaceuticals Ltd, a Janssen Pharmaceutical Company of Johnson & Johnson.

About UPTRAVI® (selexipag)

Selexipag, a selective prostacyclin IP receptor agonist, is a compound discovered by Nippon Shinyaku and licensed to Actelion Pharmaceuticals Ltd outside Japan. It is licensed for the oral treatment of PAH in more than 60 countries.

About the UPTRAVI® IV Study

The UPTRAVI® IV study (NCT03187678) was a prospective, multi-center, open-label single-sequence cross–over, Phase 3 study designed to assess the safety, tolerability and pharmacokinetics of temporarily switching between oral UPTRAVI® and UPTRAVI® IV in 20 patients. The study examined switching from a stable dose of UPTRAVI® tablets to a corresponding dose of UPTRAVI® IV and back to UPTRAVI® tablets. The treatment and observation phase was divided into three periods. In Period 1, patients received their stable oral dose of UPTRAVI® twice daily (morning and evening of Day 1). In Period 2, patients received three infusions of corresponding UPTRAVI® IV doses (morning and evening of Day 2, and morning of Day 3). In Period 3, patients resumed their stable oral UPTRAVI® dose twice daily in the evening of Day 3 for 9 days, which was continued through the safety follow-up. Patients were hospitalized during Periods 1 and 2.[2]

INDICATION AND IMPORTANT SAFETY INFORMATION

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 delay (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.

IMPORTANT SAFETY INFORMATION

- **Do not take UPTRAVI® if you** take gemfibrozil because this medicine may affect how UPTRAVI® works and cause side effects
- **Before you take UPTRAVI®, tell your healthcare provider about all your medical conditions, including 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
  - 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
- Diarrhea
- Jaw pain

- Nausea
- Muscle pain
- Vomiting
- Pain, redness or swelling at the injection site with UPTRAVI® for injection
- Pain in arms or legs
- Temporary reddening of the skin (flushing)
- Joint pain
- Low red blood cell count
- Less appetite than usual
- 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 other medicines away from 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®?
UPTRAVI® Tablets
- 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

UPTRAVI® given by intravenous (IV) injection
- Your healthcare provider will give you UPTRAVI® into your vein through an intravenous (IV) line
- Your healthcare provider will decide how much UPTRAVI® for injection you will receive each day based on your current dose of UPTRAVI® tablets

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

About Pulmonary Arterial Hypertension (PAH)

PAH is a specific form of pulmonary hypertension (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 PAH and it is often fatal.[3-5] 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.[4,6]

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 and www.twitter.com/JanssenUS. Actelion Pharmaceuticals US, Inc. and Actelion Pharmaceuticals Ltd are 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 product development of UPTRAVI® IV. 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 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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1. UPTRAVI® (selexipag) full Prescribing Information. Actelion Pharmaceuticals US, Ltd.
2. Klose H, Chin KM, et al. *Respir Res* 2021; 22, 34.
3. Galiè N, Humbert M, et al. *Eur Heart J* 2016; 37:67-119.
4. Vachiéry JL, Gaine S. *Eur Respir Rev* 2012; 21:313-20.
5. Hoeper MG, Gibbs SR. *Eur Respir Rev* 2014; 23:450-7.
6. Rosanio S, Pelliccia F et al. *BioMed Research International* 2014: 743868.