News Release

Media Contact:
Shelly Orlacchio
Phone: +1 628-977-0120
sorlacch@its.jnj.com

Investor Contact:
Jen McIntyre
Phone: +1 732-524-3922

Janssen Showcases Commitment to Advancing Scientific Innovation in Pulmonary Arterial Hypertension (PAH) at CHEST 2021 Annual Meeting

Combination of clinical data and real-world evidence underscores need for earlier, accurate PAH diagnosis and timelier introduction of appropriate therapy

TITUSVILLE, N.J. – October 14, 2021 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today 11* abstracts highlighting data from its pulmonary hypertension (PH) portfolio will be presented at CHEST 2021, the annual meeting of the American College of Chest Physicians, held virtually October 17-20.

Data presentations from eight abstracts will provide additional evidence supporting the role of objective multiparameter risk assessment approaches in helping to optimize treatment and care for pulmonary arterial hypertension (PAH), as well as the impact of earlier and comprehensive therapy with UPTRAVI® (selexipag) and OPSUMIT® (macitentan). These data underscore the company's commitment to supporting the medical community to help better advance the standard of care and healthier outcomes for people with PAH.

Janssen will present a post-hoc analysis of GRIPHON (the largest randomized, controlled trial ever conducted in PAH patients) based on the Registry to Evaluate Early and Long-Term PAH Disease Management (REVEAL) Lite 2 risk calculator. The findings showed how continued risk assessment through use of objective risk calculators could be an important component of clinical management in the PAH treatment paradigm. The company will also present an analysis that used health insurance claims data from Optum's de-identified Clinformatics® Data Mart to highlight the development and evaluation of a predictive algorithm for unsatisfactory response to initial therapy among individuals with PAH.

"Our collection of data at CHEST 2021 represents the largest single-congress body of PAH scientific data by Janssen in recent history and underscores our efforts to facilitate earlier, accurate diagnosis and support timely introduction of appropriate PAH therapies," said Sean Studer**, M.D., Vice President, Medical Affairs, Janssen U.S., Pulmonary Hypertension. "We are seeking to extend the PAH survival curve by expanding our efforts and working in close collaboration with the medical community."

The eight PAH abstracts presented by Janssen at this year's annual CHEST meeting include:

UPTRAVI® Abstracts

- REVEAL Lite 2 Risk Assessment in Patients with Pulmonary Arterial Hypertension from the GRIPHON Study: A Post-Hoc Analysis Demonstrates Association of Risk Status with Long-Term Outcomes
- Clinical Characteristics of Patients with Pulmonary Arterial Hypertension and Treatment Patterns: A Real-World Analysis from SPHERE (SelexiPag: tHe usErs dRug rEgistry)

OPSUMIT® Abstracts

- Macitentan Treatment Effect in Patients with Pulmonary Arterial Hypertension Taking Spironolactone: Post-Hoc Analysis of the Phase 3 SERAPHIN Trial
- Care and Characteristics of Patients With Pulmonary Arterial Hypertension (PAH) in U.S. Clinical Practice

Risk Assessment and Diagnostics

- Development of a Simplified Risk Calculator for Stratifying Patients with Pulmonary Arterial Hypertension Based on Echocardiographic Parameters in the REVEAL Database
- Transthoracic Echocardiogram (ECHO) and Right Heart Catheterization (RHC) as Disease Management Tools for Patients with Pulmonary Arterial Hypertension (PAH) in U.S. Clinical Practice
- Comparison of Idiopathic Versus Connective Tissue Disease-Associated Pulmonary Arterial Hypertension (PAH) Groups in U.S. Clinical Practice
- Development and Evaluation of A Predictive Algorithm For Unsatisfactory Response Among Patients with Pulmonary Arterial Hypertension Using Health Insurance Claims Data

**While Janssen has 11 abstracts being presented at the CHEST Congress, this press release focuses on the eight abstracts listed above. The remaining three Janssen abstracts, looking at specific phenotypes, are:*

- A Comparison of Treatment Patterns and Healthcare Resource Utilization in Portopulmonary Hypertension and Idiopathic/Hereditary Pulmonary Arterial Hypertension in the USA
- Real-World Clinical Presentation of Patients with Portopulmonary Hypertension in Comparison with Idiopathic/Hereditary Pulmonary Arterial Hypertension in the USA
- Safety of Macitentan in Pulmonary Hypertension Patients with Elevated Pulmonary Capillary Wedge Pressure: Real-World Evidence from OPUS/OrPHeUS

To learn more about data Janssen will be presenting at CHEST 2021, please visit the CHEST website here.

**Sean Studer is an employee of Actelion Pharmaceuticals U.S., Inc., one of the Janssen Pharmaceutical Companies 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, one of the Janssen Pharmaceutical Companies of Johnson & Johnson, outside Japan. UPTRAVI® is licensed for the oral treatment of PAH in more than 60 countries. UPTRAVI® has also been approved by the U.S. Food and Drug Administration (FDA) for intravenous (IV) treatment of PAH in adult patients with WHO functional class (FC) II–III, who are temporarily unable to take oral therapy.

About OPSUMIT® (macitentan)

OPSUMIT® is indicated for the treatment of PAH (WHO Group I) to reduce the risks of disease progression and hospitalization 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.

UPTRAVI® INDICATION AND IMPORTANT SAFETY INFORMATION

INDICATION

UPTRAVI® (selexipag) is indicated for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) to delay disease progression and reduce the risk of hospitalization for PAH.

Effectiveness of UPTRAVI® Tablets was established in a long-term study in PAH patients with WHO Functional Class II-III symptoms.

Patients had idiopathic and heritable PAH (58%), PAH associated with connective tissue disease (29%), and PAH associated with congenital heart disease with repaired shunts (10%).

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Concomitant use of strong inhibitors of CYP2C8 (eg, gemfibrozil) with UPTRAVI® is contraindicated.

WARNINGS AND PRECAUTIONS

Pulmonary Edema With Pulmonary Veno-Occlusive Disease (PVOD)

Should signs of pulmonary edema occur, consider the possibility of associated PVOD. If confirmed, discontinue UPTRAVI®.

ADVERSE REACTIONS

Adverse reactions more frequent compared to placebo (≥3%) seen with UPTRAVI® Tablets are headache (65% vs 32%), diarrhea (42% vs 18%), jaw pain (26% vs 6%), nausea (33% vs 18%), myalgia (16% vs 6%), vomiting (18% vs 9%), pain in extremity (17% vs 8%), flushing (12% vs 5%), arthralgia (11% vs 8%), anemia (8% vs 5%), decreased appetite (6% vs 3%), and rash (11% vs 8%).

These adverse reactions are more frequent during the dose titration phase.

Hyperthyroidism was observed in 1% (n=8) of patients on UPTRAVI® Tablets and in none of the patients on placebo.

DRUG INTERACTIONS

CYP2C8 Inhibitors

Concomitant administration with gemfibrozil, a strong inhibitor of CYP2C8, doubled exposure to selexipag and increased exposure to the active metabolite by approximately 11-fold. Concomitant use of UPTRAVI® with strong inhibitors of CYP2C8 is contraindicated.

Concomitant administration of UPTRAVI® with clopidogrel, a moderate inhibitor of CYP2C8, had no relevant effect on the exposure to selexipag and increased the exposure to the active metabolite by approximately 2.7-fold. Reduce the dosing of UPTRAVI® to once daily in patients on a moderate CYP2C8 inhibitor.

CYP2C8 Inducers
Concomitant administration with an inducer of CYP2C8 and UGT 1A3 and 2B7 enzymes (rifampin) halved exposure to the active metabolite. Increase UPTRAVI® dose, up to twice, when co-administered with rifampin. Reduce UPTRAVI® when rifampin is stopped.

DOSAGE AND ADMINISTRATION

Recommended Dosage
Recommended starting dose is 200 mcg twice daily for UPTRAVI® Tablets. Tolerability may be improved when taken with food. Increase by 200 mcg twice daily, usually at weekly intervals, to the highest tolerated dose up to 1600 mcg twice daily. If dose is not tolerated, reduce to the previous tolerated dose.

Patients With Hepatic Impairment
For patients with moderate hepatic impairment (Child-Pugh class B), the starting dose of UPTRAVI® Tablets is 200 mcg once daily. Increase by 200 mcg once daily at weekly intervals, as tolerated. Avoid use of UPTRAVI® in patients with severe hepatic impairment (Child-Pugh class C).

Co-administration With Moderate CYP2C8 Inhibitors
When co-administered with moderate CYP2C8 inhibitors (eg, clopidogrel, deferasirox and teriflunomide), reduce the dosing of UPTRAVI® to once daily.

Dosage Strengths
UPTRAVI® tablet strengths:
200, 400, 600, 800, 1000, 1200, 1400, and 1600 mcg.

Additional Important Safety Information for UPTRAVI® for injection

Use UPTRAVI® for injection in patients who are temporarily unable to take oral therapy.

Administer UPTRAVI® for injection twice daily by intravenous infusion at a dose that corresponds to the patient's current dose of UPTRAVI® Tablets (see Table 1 in full Prescribing Information). Administer UPTRAVI® for injection as an 80-minute intravenous infusion.

Adverse Reactions: Infusion-site reactions (infusion-site erythema/redness, pain and swelling) were reported with UPTRAVI® for injection.

Please see full Prescribing Information.

OPSUMIT® INDICATION AND IMPORTANT SAFETY INFORMATION

INDICATION
OPSUMIT® (macitentan) is an endothelin receptor antagonist (ERA) indicated for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) to reduce the risks of disease progression and hospitalization for PAH.

Effectiveness was established in a long-term study in PAH patients with predominantly WHO Functional Class II-III symptoms treated for an average of 2 years. Patients had idiopathic and heritable PAH (57%), PAH caused by connective tissue disorders (31%), and PAH caused by congenital heart disease with repaired shunts (8%).

IMPORTANT SAFETY INFORMATION

BOXED WARNING: EMBRYO-FETAL TOXICITY

- **Do not administer OPSUMIT® to a pregnant female because it may cause fetal harm.**
- **Females of reproductive potential: Exclude pregnancy before the start of treatment, monthly during treatment, and 1 month after stopping treatment. Prevent pregnancy during treatment and for one month after stopping treatment by using acceptable methods of contraception.**
- **For all female patients, OPSUMIT® is available only through a restricted program called the OPSUMIT® Risk Evaluation and Mitigation Strategy (REMS).**

CONTRAINDICATIONS

Pregnancy: OPSUMIT® may cause fetal harm when administered to a pregnant woman. OPSUMIT® is contraindicated in females who are pregnant. If OPSUMIT® is used during pregnancy, advise the patient of the potential risk to a fetus.

WARNINGS AND PRECAUTIONS

Embryo-fetal Toxicity and OPSUMIT® REMS Program

Due to the risk of embryo-fetal toxicity, OPSUMIT® is available for females only through a restricted program called the OPSUMIT® REMS Program. For females of reproductive potential, exclude pregnancy prior to initiation of therapy, ensure use of acceptable contraceptive methods, and obtain monthly pregnancy tests.

Notable requirements of the OPSUMIT® REMS Program include:

- Prescribers must be certified with the program by enrolling and completing training.
- All females, regardless of reproductive potential, must enroll in the OPSUMIT® REMS Program prior to initiating OPSUMIT®. Male patients are not enrolled in the REMS.
- Females of reproductive potential must comply with the pregnancy testing and contraception requirements.
- Pharmacies must be certified with the program and must only dispense to patients who are authorized to receive OPSUMIT®.

Hepatotoxicity

- ERAs have caused elevations of aminotransferases, hepatotoxicity, and liver failure. The incidence of elevated aminotransferases in the SERAPHIN study >3 x ULN was 3.4% for OPSUMIT® vs 4.5% for placebo, and >8 x ULN was 2.1% vs 0.4%, respectively. Discontinuations for hepatic adverse events were 3.3% for OPSUMIT® vs 1.6% for placebo.
- Obtain liver enzyme tests prior to initiation of OPSUMIT® and repeat during treatment as clinically indicated.
- Advise patients to report symptoms suggesting hepatic injury (nausea, vomiting, right upper quadrant pain, fatigue, anorexia, jaundice, dark urine, fever, or itching).
- If clinically relevant aminotransferase elevations occur, or if elevations are accompanied by an increase in bilirubin >2 x ULN, or by clinical symptoms of hepatotoxicity, discontinue OPSUMIT®. Consider re-initiation of OPSUMIT® when hepatic enzyme levels normalize in patients who have not experienced clinical symptoms of hepatotoxicity.

Fluid Retention

- Peripheral edema and fluid retention are known consequences of PAH and ERAs. In the pivotal PAH study SERAPHIN, edema was reported in 21.9% of the OPSUMIT® group vs 20.5% for placebo.
- Patients with underlying left ventricular dysfunction may be at particular risk for developing significant fluid retention after initiation of ERA treatment. In a small study of pulmonary hypertension due to left ventricular dysfunction, more patients in the OPSUMIT® group developed significant fluid retention and had more hospitalizations due to worsening heart failure compared to placebo. Postmarketing cases of edema and fluid retention occurring within weeks of starting OPSUMIT®, some requiring intervention with a diuretic or hospitalization for decompensated heart failure, have been reported.
- Monitor for signs of fluid retention after OPSUMIT® initiation. If clinically significant fluid retention develops, evaluate the patient to determine the cause and the possible need to discontinue OPSUMIT®.

Hemoglobin Decrease

- Decreases in hemoglobin concentration and hematocrit have occurred following administration of other ERAs and in clinical studies with OPSUMIT®. These decreases occurred early and stabilized thereafter.
- In the SERAPHIN study, OPSUMIT® caused a mean decrease in hemoglobin (from baseline to 18 months) of about 1.0 g/dL vs no change in the placebo group. A decrease in hemoglobin to below 10.0 g/dL was reported in 8.7% of the OPSUMIT® group vs 3.4% for placebo. Decreases in hemoglobin seldom require transfusion.
- Initiation of OPSUMIT® is not recommended in patients with severe anemia. Measure hemoglobin prior to initiation of treatment and repeat during treatment as clinically indicated.

Pulmonary Edema with Pulmonary Veno-occlusive Disease (PVOD)

Should signs of pulmonary edema occur, consider the possibility of associated PVOD. If confirmed, discontinue OPSUMIT®.

Decreased Sperm Counts

OPSUMIT®, like other ERAs, may have an adverse effect on spermatogenesis. Counsel men about potential effects on fertility.

ADVERSE REACTIONS

Most common adverse reactions (more frequent than placebo by ≥3%) were anemia (13% vs 3%), nasopharyngitis/pharyngitis (20% vs 13%), bronchitis (12% vs 6%), headache (14% vs 9%), influenza (6% vs 2%), and urinary tract infection (9% vs 6%).

DRUG INTERACTIONS

- Strong inducers of CYP3A4 such as rifampin significantly reduce macitentan exposure. Concomitant use of OPSUMIT® with strong CYP3A4 inducers should be avoided.
- Strong inhibitors of CYP3A4 like ketoconazole approximately double macitentan exposure. Many HIV drugs like ritonavir are strong inhibitors of CYP3A4. Avoid concomitant use of OPSUMIT® with strong CYP3A4 inhibitors. Use other PAH treatment options when strong CYP3A4 inhibitors are needed as part of HIV treatment.
- Moderate dual inhibitors of CYP3A4 and CYP2C9 such as fluconazole and amiodarone are predicted to increase macitentan exposure. Avoid concomitant use of OPSUMIT® with moderate dual inhibitors of CYP3A4 and CYP2C9.
- Concomitant treatment of both a moderate CYP3A4 inhibitor and moderate CYP2C9 inhibitor with OPSUMIT® should also be avoided.

Please see full Prescribing Information, including BOXED WARNING.

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.[1-3] 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.[2,4]

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 OPSUMIT® (macitentan) product development. 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, 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.

# # #

1. Galiè N, Humbert M, et al. *Eur Heart J* 2016; 37:67-119.
2. Vachiéry JL, Gaine S. *Eur Respir Rev* 2012; 21:313-20.
3. Hoeper MG, Gibbs SR. *Eur Respir Rev* 2014; 23:450-7.
4. Rosanio S, Pelliccia F et al. *BioMed Research International* 2014: 743868.