



PRESS RELEASE

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Actelion Submits Supplemental New Drug Application to US FDA Seeking Approval of OPSUMIT® (macitentan) for the Treatment of Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

Filing supported by data from MERIT-1 trial evaluating OPSUMIT in adults with inoperable CTEPH which showed significant improvements in pulmonary vascular resistance and six-minute walk distance (6MWD) compared with ongoing background therapy

CHERRY HILL, NJ, AND ALLSCHWIL, SWITZERLAND – April 30, 2018 – Actelion Pharmaceuticals Ltd, one of the Janssen Pharmaceutical Companies of Johnson & Johnson, today announced the submission of a supplemental New Drug Application (sNDA) to the U.S. Food and Drug Administration (FDA) seeking to expand the indication of OPSUMIT (macitentan) to include the treatment of adults with inoperable chronic thromboembolic pulmonary hypertension (CTEPH, WHO Group 4) to improve exercise capacity and pulmonary vascular resistance (PVR).

The filing is based on data from the MERIT-1 trial, which showed significant improvements in the primary and secondary endpoint of PVR and 6MWD, respectively, compared with background therapy. OPSUMIT was well tolerated in this patient population and safety was generally consistent with the known safety profile for OPSUMIT from previous clinical studies.¹ The study results were presented at the American Thoracic Society (ATS) 2017 and European Respiratory Society (ERS) 2017 and published in [The Lancet Respiratory Medicine](#).

A substantial proportion (almost 40%) of CTEPH patients are deemed inoperable and current pharmacological treatment options for these patients are limited to one therapy only. MERIT-1 provides the first randomized controlled trial data involving patients on combination therapy, addressing a key unmet need in CTEPH.

Martin Fitchet, M.D., Global Head, Research & Development at Actelion Pharmaceuticals Ltd, commented: "Inoperable chronic thromboembolic pulmonary hypertension is associated with a poor prognosis if left untreated. At Actelion, we are committed to advancing therapies for pulmonary hypertension patients around the world and we believe that this application may provide a new

therapeutic option for those living with inoperable CTEPH in the United States. With this latest milestone, Actelion is continuing to build on its 20-year legacy of ground-breaking innovation in this life-limiting disease.”

OPSUMIT is an orally active endothelin receptor antagonist (ERA) that is currently approved in the U.S. for the treatment of PAH (WHO Group I) to delay disease progression and hospitalization.³

Cautions Concerning Forward-Looking Statements

This press release contains “forward-looking statements” as defined in the Private Securities Litigation Reform Act of 1995 regarding OPSUMIT (macitentan), an orally active endothelin receptor antagonist (ERA) that is currently approved in the U.S. for the treatment of PAH (WHO Group I) to delay disease progression and hospitalization. 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 December 31, 2017, including in the sections captioned “Cautionary Note Regarding Forward-Looking Statements” and “Item 1A. Risk Factors,” and in the company’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.

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Notes to the Editor

ABOUT CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION (CTEPH)

CTEPH is a unique form of pulmonary hypertension (PH) caused by chronic obstruction of the pulmonary arteries. The obstructions can result from blood clots that become stuck to the walls of the pulmonary arteries. The lining of the pulmonary arteries then begins to form excess tissue around the clots, transforming them into fibrous scar tissue that is attached to the artery wall. This creates a blockage that restricts the blood flow and increases the blood pressure, causing pulmonary hypertension and chronic stress to the right side of the heart – with the risk of developing right-side heart failure over time.⁴ CTEPH is a progressive disease that impacts approximately 1,600 new patients in the U.S. each year.⁵

Pulmonary thromboendarterectomy (PEA) remains the preferred treatment for CTEPH. However, certain CTEPH patients are not operative candidates due to the nature of the disease, location of the thrombi or multiple co-morbid conditions. New medical treatment options are therefore needed for the effective management of this patient group.⁶

ABOUT ENDOTHELIN RECEPTOR ANTAGONISTS (ERAs)

Macitentan is an oral ERA, which is a medication that helps patients with PAH by blocking the effects of the extra endothelin their bodies produce. Endothelin is a naturally occurring chemical in the body and is involved in blood flow.³

However, patients with PAH have levels of endothelin that are higher than normal. Researchers have found that too much endothelin can cause blood vessels to tighten. It is more difficult for blood to flow through tightened blood vessels, and this can affect how the heart works.⁷

ABOUT THE MERIT-1 STUDY¹

MERIT-1 (Macitentan in the treatment of Inoperable chronic Thromboembolic pulmonary hypertension) is a Phase II prospective, randomized, placebo-controlled, double-blind, multicenter, parallel-group study to assess the efficacy, safety and tolerability of 10 mg macitentan in patients with inoperable CTEPH.

In MERIT-1, 80 inoperable patients were randomized in a 1:1 ratio into 2 treatment groups (macitentan 10mg or placebo) over a 24-week treatment period. The study started in August 2014 and was completed in September 2016. Patients with symptomatic PH in WHO Functional Class (FC) III or IV at baseline were allowed to receive PH background therapy throughout the study, including PDE5 inhibitors or oral/inhaled prostanoids. All patients included into the study underwent independent operability assessment based on local or central adjudication committees.

After 16 weeks of treatment, there was a significant reduction in PVR for macitentan compared with placebo (mean [SD] decrease from baseline -206 [450.4] dyn·s/cm⁵ vs. -86 [301.5]; $p=0.041$). The efficacy observed was consistent across all sub-groups, including patients receiving background PAH specific therapy at baseline (61% of patients), including PDE5 inhibitors (59% of patients).

The study also showed a significant positive effect of macitentan compared to placebo on exercise capacity. After 24 weeks of treatment, the mean change in 6MWD from baseline was an increase of 35 meters in macitentan and 1 meter in placebo. The 6MWD least squares mean increase at Week 24 was 34.0 meters between macitentan and placebo (95% CL: 2.9, 65.2 m; $p=0.03$).

Macitentan was well tolerated in this patient population and safety was in general consistent with the known safety profile for macitentan from previous clinical studies. The most frequently ($\geq 10\%$) reported adverse events that occurred with higher frequency on macitentan vs. placebo were peripheral edema (23% vs. 10.0%) and decrease in hemoglobin (15% vs. 0%).

ABOUT OPSUMIT (macitentan)

OPSUMIT, an orally available endothelin receptor antagonist, resulted from a tailored drug discovery process in Actelion's laboratories.

In the U.S., OPSUMIT is indicated for the treatment of PAH, WHO Group I to delay disease progression.⁴

Disease progression included: death, initiation of intravenous (IV) or subcutaneous prostanoids, or clinical worsening of PAH (decreased 6-minute walk distance, worsened PAH symptoms and need for additional PAH treatment). OPSUMIT also reduced hospitalization for PAH.⁴

Effectiveness was established in a long-term study in PAH patients with predominantly WHO FC II-III symptoms treated for an average of 2 years. Patients were treated with OPSUMIT monotherapy or in combination with PDE5 inhibitors or inhaled prostanoids. 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%).³

In Europe, OPSUMIT is indicated, as monotherapy or in combination, for the long-term treatment of PAH in adult patients of WHO Functional Class (FC) II to III. Efficacy has been shown in a PAH population including idiopathic and heritable PAH, PAH associated with connective tissue disorders, and PAH associated with corrected simple congenital heart disease.⁸

OPSUMIT is very likely to cause major birth defects. It is contraindicated for use in pregnancy. In the U.S., OPSUMIT is distributed under a risk evaluation and mitigation strategy (REMS).³

ABOUT ACTELION

In June 2017, Actelion became part of the Janssen Pharmaceutical Companies of Johnson & Johnson. Actelion's medicines have helped to expand and strengthen Janssen's portfolio with leading, differentiated in-market medicines and promising late-stage compounds. Janssen has added Pulmonary Hypertension as a therapeutic area of focus to maintain the leadership position Actelion has built in this important disease area.

ABOUT THE JANSSEN PHARMACEUTICAL COMPANIES OF JOHNSON & JOHNSON

At the Janssen Pharmaceutical Companies of Johnson & Johnson, we are working to create a world without disease. Transforming lives by finding new and better ways to prevent, intercept, treat and cure disease inspires us. We bring together the best minds and pursue the most promising science. We are Janssen. We collaborate with the world for the health of everyone in it. Learn more at www.janssen.com. Follow us at www.twitter.com/JanssenUS and www.twitter.com/JanssenGlobal.

Actelion, a leader in Pulmonary Hypertension, is part of the Janssen Pharmaceutical Companies of Johnson & Johnson. Learn more at www.actelion.com. Follow us at [@actelion_com](https://twitter.com/actelion_com)

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