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# Investor News

**Not intended for U.S. and UK Media**

## Bayer's Riociguat for Patients with Chronic Thromboembolic Pulmonary Hypertension and Pulmonary Arterial Hypertension Submitted For Regulatory Approval in the U.S. and EU

Riociguat is the first drug that has consistently demonstrated efficacy in two life-threatening PH indications – chronic thromboembolic pulmonary hypertension (CTEPH) and pulmonary arterial hypertension (PAH)

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**Leverkusen, February 11, 2013 –** Bayer HealthCare has submitted the oral investigational drug riociguat to treat patients with inoperable chronic thromboembolic pulmonary hypertension (CTEPH) and pulmonary arterial hypertension (PAH) for regulatory approval in the United States and in the European Union.

"These regulatory submissions for two distinct forms of pulmonary hypertension not only represent important progress in our cardiovascular pipeline but also fuel our hope to bring this much-needed new treatment option for these serious and potentially fatal diseases to patients and doctors soon," said Kemal Malik, member of the Bayer HealthCare Executive Committee and Head of Global Development.

Riociguat was discovered by Bayer and represents the first member of a novel class of compounds, the stimulators of soluble guanylate cyclase (sGC). Riociguat is the first drug to demonstrate clinical efficacy in a placebo controlled phase III trial in inoperable CTEPH patients.

The submission is supported by data from the two pivotal, global Phase III studies namely CHEST-1 and PATENT-1. Results of both studies were presented at the 2012 annual meeting of the American College of Chest Physicians (ACCP) in Atlanta, USA. Both Phase III studies on riociguat met their primary endpoint in exercise capacity. Riociguat was generally well tolerated, with no unexpected adverse events reported.

In CHEST-1 patients treated with riociguat showed a statistically significant improvement ($p<0.0001$) from baseline in the six-minute walking test (6MWT) after 16 weeks, compared to those receiving placebo. The study included both patients with inoperable CTEPH and those with persistent or recurrent disease after a surgical procedure called pulmonary endarterectomy (PEA). The PATENT-1 study met its primary endpoint by demonstrating a statistically significant improvement ($p<0.0001$) from baseline in the 6MWT, after 12 weeks compared with placebo. PATENT-1 included both treatment naïve symptomatic PAH patients and those pre-treated with ERAs or non-iv prostanoid monotherapy.

**About Pulmonary Hypertension**

Pulmonary hypertension (PH) is a severe, progressive and life-threatening disorder in which the pressure in the pulmonary arteries is significantly increased due to vasoconstriction and which can lead to heart failure and death. Patients with PH develop a markedly decreased exercise tolerance and reduced quality of life. The most common symptoms of PH include shortness of breath, fatigue, dizziness and fainting, all of which are worsened by exertion. As the symptoms of PH are non-specific, diagnosis can be delayed by as much as two years. Early diagnosis is essential as a delay in treatment initiation can have a negative impact on survival. Continuous treatment monitoring is then vital to ensure that patients are receiving optimal care for their particular type and stage of disease.

According to the clinical classification of PH (Dana Point), there are five different types of PH based on underlying causes which are: pulmonary arterial hypertension (PAH), pulmonary hypertension owing to left heart disease (e.g. PH-LVD), pulmonary hypertension owing to lung disease and/or hypoxemia (e.g. PH-COPD or PH-ILD), chronic thromboembolic pulmonary hypertension (CTEPH) and pulmonary hypertension with unclear multifactorial mechanisms. Currently available pharmacological treatments are only approved to treat one of the five types of PH, pulmonary arterial hypertension. As a result there is a strong need for more research to improve understanding of how all five types of PH can be treated effectively.

**About Pulmonary Arterial Hypertension (PAH)**

PAH is a rare but life-threatening disease in which the pressure in the pulmonary arteries is above normal. PAH is characterized by morphological changes to the endothelium of the arteries of the lungs causing remodelling of the tissue, vasoconstriction and thrombosis-in-situ. As a result of these changes, the blood vessels in the lungs are

narrowed making it difficult for the heart to pump blood through to the lungs. PAH affects an estimated 52 people per million globally. It is more prevalent in younger women than men. In most cases PAH has no known cause and, in some cases, it can be inherited.

Despite the availability of several approved therapies, the prognosis for patients with PAH remains poor.

**About Chronic Thromboembolic Pulmonary Hypertension (CTEPH)**
CTEPH is a rare but life-threatening disease in which it is believed that thromboembolic occlusion (blood clots) of pulmonary vessels gradually lead to an increased pressure in the pulmonary arteries, resulting in an overload of the right heart. CTEPH may evolve after prior episodes of acute pulmonary embolism, but the pathogenesis is not yet completely understood. The standard treatment for CTEPH is pulmonary endarterectomy (PEA), a surgical procedure in which the blood vessels of the lungs are cleared of clot and scar material. However, a considerable number of patients with CTEPH are not operable and in some patients the disease persists or reoccurs after PEA. Currently, there are no approved pharmacological treatments available for CTEPH.

**About Riociguat**
Riociguat (BAY 63-2521) is an oral agent being investigated as a new approach to treating different types of pulmonary hypertension. Riociguat is the first member of a novel class of compounds, the stimulators of soluble guanylate cyclase (sGC). sGC is an enzyme found in the cardiopulmonary system. When nitric oxide (NO) binds to sGC, the enzyme catalyzes synthesis of the signaling molecule cyclic guanosine monophosphate (cGMP). cGMP plays an important role in regulating vascular tone, proliferation, fibrosis, and inflammation.

Pulmonary hypertension is associated with endothelial dysfunction, impaired synthesis of NO and thus insufficient stimulation of the NO-sGC-cGMP pathway. Riociguat is believed to have a dual mode of action: sensitizing sGC to endogenous NO and also directly stimulating sGC independent of NO.

**About Bayer HealthCare**
The Bayer Group is a global enterprise with core competencies in the fields of health care, agriculture and high-tech materials. Bayer HealthCare, a subgroup of Bayer AG with annual sales of EUR 17.2 billion (2011), is one of the world’s leading, innovative companies in the healthcare and medical products industry and is based in Leverkusen,

Germany. The company combines the global activities of the Animal Health, Consumer Care, Medical Care and Pharmaceuticals divisions. Bayer HealthCare's aim is to discover, develop, manufacture and market products that will improve human and animal health worldwide. Bayer HealthCare has a global workforce of 55,700 employees (Dec 31, 2011) and is represented in more than 100 countries. More information at www.healthcare.bayer.com.

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