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Investor News

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Bayer's Riociguat Recommended for Approval in the EU in Two Forms of Pulmonary Hypertension

- Riociguat is the first drug to consistently demonstrate efficacy in two life-threatening pulmonary hypertension (PH) indications – chronic thromboembolic pulmonary hypertension (CTEPH) and pulmonary arterial hypertension (PAH)
- Riociguat has been developed to target a key molecular mechanism underlying this serious disorder of the heart and lungs

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Leverkusen, Germany, January 24, 2014 – The European Committee for Medicinal Products for Human Use (CHMP) today recommended approval for riociguat tablets for use in two forms of pulmonary hypertension, a group of life-threatening and progressive diseases: The treatment of adult patients with inoperable chronic thromboembolic pulmonary hypertension (CTEPH) or persistent or recurrent CTEPH after surgical treatment to improve exercise capacity, and the treatment of adult patients with pulmonary arterial hypertension (PAH) to improve exercise capacity. Riociguat is the first of a novel class of drugs, the soluble guanylate cyclase (sGC)-stimulators. Its new mode of action has been developed to target a key molecular mechanism underlying pulmonary hypertension. The final decision of the European Commission on the approval is expected in the first half of 2014.

"We appreciate today's recommendation by the CHMP to approve riociguat, and we look forward to bringing riociguat to patients with these rare, serious and life-threatening diseases upon approval of the European Commission," said Kemal Malik (MB, BS), Member of the Bayer HealthCare Executive Committee and Head of Global Development. "Riociguat is the first drug to demonstrate efficacy in two forms of pulmonary hypertension, PAH and CTEPH. For CTEPH, pulmonary endarterectomy is the primary and potentially curative treatment option. There is no drug treatment approved to date in the European Union – however, a considerable number of CTEPH

patients are not operable, and in up to 35% of operated patients the disease persists or reoccurs."

"The consistency and robustness of the positive results from the clinical trial programs CHEST and PATENT are substantial: Riociguat has demonstrated significant and sustained clinical efficacy and safety in treatment-naïve PAH patients and patients pre-treated with endothelin-receptor antagonists (ERAs) or prostanoid monotherapy, as well as in patients with inoperable CTEPH or persistent or recurrent CTEPH after surgery. So far no other pharmacological treatment has shown significant effect in CTEPH," said Principal Investigator Professor Ardeschir Ghofrani, University Hospital Giessen and Marburg, Germany. "For both PAH and CTEPH patients and their treating physicians, the clinical improvements across multiple endpoints such as 6 Minute Walking Distance, cardiopulmonary hemodynamics, WHO Functional Class and a disease-related biomarker in the treatment with riociguat are of high relevance."

The CHMP recommendation is based on results from the two randomized, double-blind, placebo-controlled, global Phase III studies CHEST-1 and PATENT-1 as well as on interim results of the long-term extension studies CHEST-2 and PATENT-2 available at the time. These assessed the efficacy and safety of oral riociguat in the treatment of CTEPH and PAH respectively. PAH and CTEPH are two rare and life-threatening forms of pulmonary hypertension characterized by significantly increased pressure in the pulmonary arteries.
Both Phase III studies with riociguat met their primary endpoint, a change in exercise capacity, after 16 and 12 weeks respectively. Riociguat also demonstrated consistent improvements across multiple, relevant secondary endpoints, and was generally well-tolerated, with a good safety profile. Results of both studies were published in the New England Journal of Medicine (NEJM) in July 2013. The Phase III trial programs CHEST and PATENT are ongoing with the long-term extension studies, CHEST-2 and PATENT-2, showing in first interim analyses a good safety profile and sustained efficacy over one year. The most commonly reported adverse reactions, occurring in greater than or equal to 10 percent of patients under riociguat treatment (up to 2.5 mg TID), were headache, dizziness, dyspepsia, peripheral edema, nausea, diarrhea, and vomiting.

Riociguat was approved under the name Adempas® in the US for use in CTEPH and PAH in October 2013, and in Canada and Switzerland in the CTEPH indication in September and November 2013, as well as in Japan in CTEPH in January 2014. In February 2013,

Bayer HealthCare submitted riociguat for regulatory approval in the European Union in both indications.

About Pulmonary Hypertension

Pulmonary hypertension (PH) is a severe, progressive, life-changing and life-threatening disorder of the heart and lungs in which the blood pressure in the pulmonary arteries is above normal, and which can lead to heart failure and death. Patients with PH develop a markedly decreased exercise capacity and a 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 and accurate identification of the PH type are 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.

There are five different types of PH; each can affect the patient in a different way and every patient may have a different etiology and manifestation of PH. For the best chance of success patients need to be treated at a PH specialist center.

About Pulmonary Arterial Hypertension (PAH)

PAH, one of the five types of pulmonary hypertension (PH), is a progressive and life-threatening disease in which the blood pressure in the pulmonary arteries is significantly increased due to vasoconstriction and which can lead to heart failure and death. PAH is characterized by morphological changes to the endothelium of the artery of the lungs causing remodeling 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 is a rare disease and affects an estimated 15-52 people per million globally. It is more prevalent in women than men. In most cases, PAH has no known cause and, in some cases, it can be inherited.

In spite of several pharmacological treatment options for PAH having been available for over a decade, the prognosis for these patients has remained poor and so new treatment options are needed. Currently, mortality of PAH patients remains high and is still 15% at 1 year and 32% at 3 years after diagnosis.

About Chronic Thromboembolic Pulmonary Hypertension (CTEPH)
CTEPH is a progressive and life-threatening disease and a type of PH, in which it is believed that thromboembolic occlusion (organized blood clots) of pulmonary vessels gradually lead to an increased blood pressure in the pulmonary arteries, resulting in an overload of the right heart. CTEPH is a rare disease and is comparable in terms of population size to PAH. CTEPH may evolve after prior episodes of acute pulmonary embolism, but the pathogenesis is not yet completely understood. The standard and potentially curative 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 (20%-40%) are not operable and in up to 35% of patients, the disease persists or reoccurs after PEA. These patients need an effective pharmacological treatment.

About Riociguat
Riociguat is a soluble guanylate cyclase (sGC) stimulator, the first member of a novel class of compounds, discovered and developed by Bayer as an oral treatment to target a key molecular mechanism underlying PH. Riociguat is being investigated as a new and specific approach to treat different types of PH. sGC is an enzyme found in the cardiopulmonary system and the receptor for nitric oxide (NO). When NO binds to sGC, the enzyme enhances synthesis of the signaling molecule cyclic guanosine monophosphate (cGMP). cGMP plays an important role in regulating vascular tone, proliferation, fibrosis, and inflammation.

PH is associated with endothelial dysfunction, impaired synthesis of NO and insufficient stimulation of sGC. Riociguat has a novel mode of action – it sensitizes sGC to endogenous NO by stabilizing the NO-sGC binding. Riociguat also directly stimulates sGC via a different binding site, independently of NO. Riociguat, as a stimulator of sGC, addresses the issue of NO deficiency by restoring the NO-sGC-cGMP pathway, leading to increased generation of cGMP.

With its novel mode of action, Riociguat has the potential to overcome a number of limitations of currently approved PAH therapies, including NO dependence, and is the first drug which has shown clinical benefits in CTEPH, where no pharmacological treatment is approved.

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 18.6 billion (2012), 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 54,900 employees (Dec 31, 2012) and is represented in more than 100 countries. More information at www.healthcare.bayer.com.

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