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Investor News

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Bayer to Evaluate Riociguat in New Indication

Phase IIb Study Initiated to Investigate Riociguat in Pulmonary Hypertension associated with Idiopathic Interstitial Pneumonia

Leverkusen, Germany, June 3, 2014 – Bayer HealthCare announced today the start of a randomized, double-blind, placebo-controlled Phase IIb study. The RISE-IIP study (Riociguat in Patients with Symptomatic Pulmonary HypErtension associated with Idiopathic Interstitial Pneumonias) is designed to investigate the efficacy and safety of riociguat in patients with symptomatic pulmonary hypertension (PH) associated with idiopathic interstitial pneumonia (IIP).

Pulmonary hypertension is a co-morbidity seen in 30%-85% of patients with idiopathic interstitial pneumonia (IIP) and is associated with increased mortality. Once diagnosed, the median survival time in PH-IIP patients is estimated to be 2.5 to 3.5 years. Initially, patients may present with non-specific symptoms like dry cough and shortness of breath, so that the diagnosis of PH is often delayed. The clinical symptoms and signs of PH usually appear late in the course of IIP, so that they are often masked by this underlying pulmonary disorder.

“The RISE-IIP study is of great importance as it evaluates riociguat in a broad range of patients suffering from pulmonary hypertension (PH) associated with idiopathic interstitial pneumonia (IIP) – a group of patients where no approved treatment is available,” said Principal Investigator Dr. Steve Nathan, Inova Fairfax Hospital, Virginia, USA. “We hope that through this study, we will be able to provide the first clinical evidence of an effective treatment option to PH patients with different types of IIPs, for example non-specific interstitial pneumonia and unclassifiable forms of pulmonary fibrosis.”

Within the World Health Organization’s (WHO) clinical classification system for pulmonary hypertension (Dana Point 2008), PH-IIP belongs to Group 3, representing pulmonary

hypertension owing to lung diseases and/or hypoxia. Riociguat is the first drug to be approved in two pulmonary hypertension indications, namely chronic thromboembolic pulmonary hypertension (CTEPH, WHO Group 4) and pulmonary arterial hypertension (PAH, WHO Group 1). It is the objective of the RISE-IIP study to better understand the effects of riociguat in patients belonging to WHO Group 3. Due to its novel mode of action, riociguat may benefit patients with symptomatic PH associated with IIP by primarily treating the PH component of the disease, as PH is linked to an increased mortality in this patient population. In a Phase IIa proof of concept study in patients with PH associated with interstitial lung diseases (PH-ILD), riociguat was well tolerated with a good safety profile.

The RISE-IIP trial will be carried out at more than 50 sites in 11 countries and will enrol approximately 120 patients. The study is designed as a ‘signal-generating’ study which may help to better understand the disease and the effect of riociguat on it. Based on the results, further steps will be decided.

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 PH-IIP

Pulmonary Hypertension associated with Idiopathic Interstitial Pneumonia (PH-IIP) is a rare disease in which patients suffer both from pulmonary hypertension (PH) and idiopathic interstitial pneumonia (IIP). There is a significant unmet medical need for these patients as there are no approved treatments for PH-IIP. IIP is a heterogeneous group of

rare lung disorders which are included under the umbrella term interstitial lung diseases (ILD) and which are characterized by varying degrees of inflammation and scarring (lung fibrosis). The most common subgroup of IIP is idiopathic pulmonary fibrosis (IPF). Treatment options for all forms of IIP are limited.

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 nitric oxide (NO) dependence, and is the first drug which has shown clinical benefits in CTEPH, where until the approval of riociguat no pharmacological treatment was available.

The riociguat development program across different forms of PH demonstrates Bayer’s ongoing commitment to understanding this severe and life-threatening condition, with high unmet medical need, to improve the lives of people with PH.

Riociguat was approved under the name Adempas® in the US for use in CTEPH and PAH in October 2013. In Canada, the approvals for CTEPH and PAH followed in September 2013 and March 2014 respectively. In Switzerland and Japan, riociguat was approved in the CTEPH indication in November 2013, and in January 2014 respectively.

In the EU, riociguat has been granted orphan drug designation and was approved by the European Medicines Agency (EMA) under the name Adempas® for use in CTEPH and PAH in March 2014.

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 18.9 billion (2013), 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 56,000 employees (Dec 31, 2013) and is represented in more than 100 countries. More information at www.healthcare.bayer.com.

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