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Investor News

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Long-term extension study of Riociguat in patients with CTEPH:

Interim results from CHEST-2 study support benefits of Bayer's Riociguat as demonstrated in Phase III CHEST-1 study

- Riociguat showed significant and sustained improvements in six minute walking distance (6MWD) and WHO functional class (FC) in patients with inoperable or residual chronic thromboembolic pulmonary hypertension (CTEPH)[1]
- Riociguat showed good long-term safety profile[1]

Leverkusen, Germany, March 4, 2013 – Bayer HealthCare today announced positive data from the interim analysis of the on-going CHEST-2 trial with riociguat, the open-label long-term extension of the pivotal Phase III study CHEST-1, at the 5th World Symposium of Pulmonary Hypertension (WSPH) in Nice, France. The results of the CHEST-2 trial support the positive data of the pivotal CHEST-1 trial, showing long-term safety and sustained clinical benefits in patients with inoperable chronic thromboembolic pulmonary hypertension (CTEPH) or with persistent or recurrent CTEPH after a surgical procedure called pulmonary endarterectomy (PEA).[1]

In the first interim analysis in CHEST-2, riociguat was shown to be well tolerated with a good long-term safety profile in patients with CTEPH. The most frequent drug-related adverse events were dizziness, dyspepsia and hypotension.[1]

After 12 weeks in CHEST-2, the six minute walking distance (6MWD) had increased by 63 meters in former riociguat patients and 35 meters in former placebo patients compared with baseline of the pivotal CHEST-1 trial. Also WHO functional class (FC) had improved in both patient groups. Sustained effects in 6MWD and WHO FC have been observed in a cohort of patients that had reached one year of study treatment.[1]

The lead author for the presentation of the data at the WSPH was Gérald Simonneau, Professor of Pneumology and Head of the Department of Pulmonary Disease at Hôpital Bicêtre, Le Kremlin-Bicêtre, University Paris-Sud, France.

“The interim results of CHEST-2 support the benefits of riociguat that were seen in the CHEST-1 trial and we are confident that, together, these results reinforce the role of riociguat, if approved, in treating this life-threatening disease for which no approved drug treatment is available,” said Kemal Malik, member of the Bayer HealthCare Executive Committee and Head of Global Development.

About CHEST-2 interim results

CHEST-2 is the open-label long-term extension trial of the multi-center, multi-national CHEST Phase III study program currently being conducted in 26 countries. In the randomized, double-blinded, placebo controlled pivotal CHEST-1 trial, patients with inoperable CTEPH, or persistent or recurrent CTEPH after surgery received over 16 weeks either placebo or riociguat.[2] Approximately 90% of patients from CHEST-1 entered the CHEST-2 trial which aimed to investigate the longer term safety profile of riociguat in CTEPH patients as primary outcome. In addition the sustainability of the efficacy results of CHEST-1 including 6MWD and WHO FC were measured as secondary outcomes.

The first interim analysis in CHEST-2 showed that riociguat was well-tolerated with a good long-term safety profile in patients with inoperable CTEPH and in those with persistent or recurrent disease after PEA. Adverse events were reported in 173 (89%) of patients during CHEST-2, of which 83 (43%) patients developed drug –related adverse events.The most frequent drug-related adverse events (>5%) were dizziness (8%), dyspepsia (7%) and hypotension (6%). Serious adverse events were reported by 59 (30%) patients, of which eight (4%) were considered drug related by the investigator.[1]

After 12 weeks in CHEST-2, the 6MWD had increased by 63 meters (former riociguat) and 35 meters (former placebo) against CHEST-1 baseline. In the cohort of patients that have reached one year of study treatment the increase in 6MWD was 48 meters compared with CHEST-1 baseline.[1] However, this promising result must be interpreted with caution until the complete 1-year data set for the overall population in CHEST-2 is available.

After 12 weeks in CHEST-2, improvement in WHO FC was observed in 41% and 38 % of former ricoguat and former placebo groups respectively. In the cohort of patients that have reached one year of study treatment, WHO FC had improved in 51%, stabilized in 47% and worsened in 2% of patients compared with CHEST-1 baseline.[1] Again, this promising result must be interpreted with caution until the complete 1-year data set for the overall patient population is available.

Improvements in 6MWD and WHO FC were seen consistently in both subgroups of inoperable CTEPH patients and those with persistent or recurrent CTEPH after PEA.[1]

At one year, 97% of patients in CHEST-2 were still alive and 87% were free from clinical worsening.[1]

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).[3] 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.[3]

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.[4]

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 55,300 employees (Dec 31, 2012) and is represented in more than 100 countries. More information at www.healthcare.bayer.com.

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[1] Simonneau G *et al*.Riociguat for the treatment of chronic thromboembolic pulmonary hypertension (CTEPH): A Phase III long-term extension study (CHEST-2). 5th World Symposium of Pulmonary Hypertension (WSPH) 2013, Nice, France. Poster Presentation.

[2] Ghofrani, HA. et al. Riociguat for the treatment of inoperable chronic thromboembolic pulmonary hypertension: a randomized, double-blind, placebo-controlled study (CHEST-1). ACCP 2012, Atlanta, USA. Oral abstract 1462924.

[3] Ghofrani, HA. *et al*. Riociguat for pulmonary hypertension. Furture Cardiol. 2010;6(10):155-166.

[4] Schermuly, R *et al*. Riociguat for the treatment of pulmonary hypertension. *Expert Opin Investig Drugs*. 2011 Apr;20(4):567-76.