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Investor News

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American Thoracic Society International Conference, Philadelphia, USA:

Bayer Presents Positive Interim Results from Long-term Extension Study PATENT-2 with Riociguat

- Riociguat showed good long-term safety profile[1]
- Riociguat demonstrated significant and sustained improvements in six minute walking distance (6MWD) and WHO functional class (FC) in patients with pulmonary arterial hypertension (PAH)[1]

Leverkusen, Germany, May 20, 2013 – Bayer HealthCare today announced positive data from the interim analysis of the on-going PATENT-2 trial with riociguat, the open-label long-term extension of the pivotal Phase III study PATENT-1, at the American Thoracic Society International Conference, Philadelphia, USA.[1] The results support the positive data of the pivotal PATENT-1 trial, showing long-term safety and sustained clinical benefits in patients with pulmonary arterial hypertension (PAH).[1]

“Despite the availability and advantages of several approved PAH therapies, the prognosis for patients remains poor and mortality remains high. The interim results of PATENT-2 support the benefits of riociguat that were seen in the PATENT-1 trial. We are confident that, together, these results reinforce the role of riociguat, if approved, as a new treatment in the armamentarium against PAH,” said Kemal Malik, member of the Bayer HealthCare Executive Committee and Head of Global Development.

In the first interim analysis of PATENT-2, riociguat was shown to be well tolerated with a good long-term safety profile in both treatment-naïve and pre-treated PAH patients.[1] The most frequent drug-related adverse events were headache, dizziness, dyspepsia, and hypotension.[1]

Further improvements in six minute walking distance (6MWD) were seen with continued riociguat treatment. After an additional 12 weeks of treatment in PATENT-2, the 6MWD had increased further in former riociguat patients compared with baseline of the pivotal PATENT-1 trial. The former placebo patients improved to a similar extent.[1, 2]

Functional class also improved further with continued riociguat treatment. 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 presentation of these positive data follows the recent priority review granted to riociguat by the U.S. Food and Drug Administration for its U.S. approval.

About the PATENT-2 interim results

PATENT-2 is the open-label long-term extension trial of the multi-center, multi-national PATENT Phase III study program currently being conducted in 30 countries.[1] In the randomized, double-blinded, placebo controlled pivotal PATENT-1 trial, treatment-naïve or pre-treated PAH patients received over 12 weeks either placebo or riociguat in two different dose titration arms, an individual and an exploratory capped dose titration arm.[2] Approximately 90% of patients from PATENT-1 entered the PATENT-2 trial, which aims to investigate the longer term safety profile of riociguat in PAH patients as primary outcome.[1] In addition, the sustainability of the efficacy results of PATENT-1 including 6MWD and WHO FC were measured as secondary outcomes.[1, 2]

During the initial 8-week double-blinded sham titration period of PATENT-2, patients in the riociguat individual titration arm continued on their optimum dose (up to 2.5 mg three times daily [tid]); patients in the capped dose titration arm (up to 1.5 mg tid) and placebo arms were titrated to their optimum dose of riociguat (up to 2.5 mg tid).[1]

The first interim analysis in PATENT-2 showed that riociguat was well tolerated with a good long-term safety profile as monotherapy or in combination with endothelin receptor antagonists (ERAs) or non-intravenous prostanoids.[1] Adverse events were reported in 334 (92%) of patients during PATENT-2, of which 185 (51%) patients developed drug-related adverse events.[1] The most frequent drug-related adverse events (>5%) were headache (8%), dizziness (8%), dyspepsia (7%), hypotension (5%). Serious adverse events were reported by 140 (39%) patients, of which 17 (5%) were considered drug-related by the investigator.[1]

After 12 weeks in PATENT-2, the 6MWD had increased by 53 meters (former individual titration arm of riociguat), 54 meters (former capped dose titration arm of riociguat) and 42 meters (former placebo arm) against PATENT-1 baseline.[1] In the cohort of patients that have reached one year of study treatment, the increase in 6MWD was 48 meters compared with PATENT-1 baseline.[1, 2] However, this promising result must be interpreted with caution until the complete 1-year data set for the overall population in PATENT-2 is available.

After 12 weeks in PATENT-2, improvement in WHO FC was recorded in 34%, 33% and 22% of the former individual titration arm of ricoguat, the former capped-dose titration arm of riociguat and the former placebo arm respectively.[1] In the cohort of patients that have reached one year of study treatment, WHO FC had improved in 36%, stabilized in 58% and worsened in 7% of patients compared with PATENT-1 baseline.[1, 2] Again, this promising result must be interpreted with caution until the complete 1-year data set for the overall patient population is available.

At one year, 96% of patients in PATENT-2 were still alive and 86% were free from clinical worsening. Overall, 46 (13%) patients received an additional PH medication during PATENT-2.[1]

About Pulmonary Arterial Hypertension (PAH)

PAH is a rare and 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 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 affects an estimated 52 people per million globally.[3] It is more prevalent in younger women than men.[3] In most cases, PAH has no known cause and, in some cases, it can be inherited.[4]

Despite the availability of several approved therapies, the prognosis for patients with PAH remains poor.[5]

About Riociguat

Riociguat (BAY 63-2521) is a soluble guanylate cyclase (sGC) stimulator, the first member of a novel class of compounds being investigated as a new and specific approach to treat different types of PH.[6] 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.[6]

PH is associated with endothelial dysfunction, impaired synthesis of NO and insufficient stimulation of sGC. Riociguat has a unique 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 NO deficiency by restoring the NO-sGC-cGMP pathway, leading to increased generation of cGMP.[7]

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.[7,8]

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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