American Thoracic Society (ATS) congress, San Diego, USA:

Bayer Schering Pharma presents positive results of phase II study with Riociguat

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Positive data from a phase II trial with Bayer Schering Pharma's oral agent riociguat (BAY 63-2521) in chronic thromboembolic pulmonary hypertension (CTEPH) and pulmonary arterial hypertension (PAH) were presented today at the American Thoracic Society (ATS) international conference in San Diego, USA. Riociguat is the first member of a new class of vasodilating agents called soluble guanylate cyclase (sGC) stimulators and is being investigated as a new approach for the treatment of different forms of pulmonary hypertension (PH).

Results from the multicenter, open-label, uncontrolled phase II trial, showed that riociguat significantly improved exercise capacity from baseline values in patients with CTEPH and PAH. Riociguat also demonstrated strong and significant effects on pulmonary hemodynamics and symptoms in patients with CTEPH and PAH.

"Bayer Schering Pharma aims to lead the way in advancing cardio-pulmonary research to address the significant unmet medical need for innovative treatment options in this field." said Kemal Malik, M.D., Head of Global Development and member of the Executive Committee of Bayer HealthCare. "The data presented at the ATS meeting serve to further reinforce our expectations for riociguat in patients with CTEPH and PAH".

"Pulmonary hypertension is a severe and life-threatening disease that progresses rapidly and, despite advances in patient care over the last few years, there is a real need for more efficient therapies." said lead investigator Prof. Hossein Ardeschir Ghofrani, Head of the Pulmonary Hypertension Division, Department of Internal Medicine, University of Giessen, Germany. "These findings are a positive step towards improving treatment options for PH patients – the majority of whom are currently still without viable treatment options – and could result in a significant enhancement to the care physicians currently offer their patients."

The data presentation at ATS follows an earlier presentation of positive topline phase II findings at the Annual Congress of the European Respiratory Society (ERS) in October 2008. Based on these data, randomized placebo-controlled phase III trials in CTEPH (CHEST-1, followed by an open-label extension trial, CHEST-2) and PAH (PATENT-1, followed by an open-label extension trial, PATENT-2) were initiated in December 2008, with first results from the study program currently expected in 2011. In addition to the CHEST and PATENT trials, further phase II studies of riociguat in patients suffering from other forms of PH, such as PH secondary to interstitial lung disease (PH-ILD), are ongoing. First results from the PH-ILD study are currently expected in 2009.

About the Riociguat Phase II Study in CTEPH and PAH

The phase II trial for riociguat was a 12-week, multicenter, open-label, uncontrolled study conducted in 75 patients suffering from CTEPH or PAH. Riociguat was given orally three times daily for 12 weeks. Doses were titrated at two week intervals, and patients who completed the study were offered long-term treatment with riociguat. Patients' exercise capacity was measured by the "six-minute walk test" (6-MWT), a standard test that has been used as a primary endpoint in previous pivotal clinical studies in patients with pulmonary hypertension.

Riociguat resulted in clinically relevant and significant improvements in walked distance from baseline in the 6-MWT that were evident as early as 14 days after initiating treatment in PAH and CTEPH patients. Similar improvements were found in treatment-naïve patients and patients also on an endothelin receptor antagonist (bosentan), at baseline. In addition, riociguat exerted strong and significant effects on pulmonary hemodynamics, echocardiographic parameters, and N-terminal prohormone brain natriuretic peptide (NT-proBNP) levels. Improvements were also observed in New York Heart Association (NYHA) functional class and Borg dyspnea score. In the study, riociguat was well tolerated and had a favorable safety profile. Three patients discontinued riociguat because of adverse events. Only one serious adverse event (pulmonary edema in PVOD) occurred that was considered drug related. No drug-induced changes in laboratory parameters were observed.

About the Riociguat Phase III Studies in CTEPH and PAH

The riociguat phase III program in CTEPH and PAH consists of four trials, two per indication (one pivotal trial and one extension trial, respectively):
Chronic Thrombo**e**mbolic Pulmonary Hypertension sGC-**S**timulator **T**rial (CHEST):
The randomized, placebo-controlled pivotal trial, CHEST-1, investigates the efficacy and safety of riociguat in patients with inoperable CTEPH. The primary outcome measure after 16 weeks of treatment will be patient's exercise capacity, measured by the change from baseline in the 6-MWT. All patients having completed CHEST-1 will be offered the option to enter the open label extension trial, CHEST-2, after the initial treatment duration of 16 weeks.

Pulmonary **A**rterial Hyper**ten**sion sGC-Stimulator **T**rial (PATENT):
The randomized, placebo-controlled pivotal trial, PATENT-1, investigates the efficacy and safety of riociguat in patients with PAH. The primary outcome measure after 12 weeks of treatment will be patient's exercise capacity, measured by the change from baseline in the 6-MWT. All patients having completed PATENT-1 will be offered the option to enter the open label extension trial, PATENT-2, after initial treatment duration of 12 weeks.
Recruitment for CHEST-1 and PATENT-1 is ongoing. The lead investigator of both trials is Prof. Ghofrani from the University Lung Centre in Giessen, Germany.

About Pulmonary Hypertension

Pulmonary Hypertension (PH) is a disorder in which the pressure in the pulmonary arteries is above normal. People with PH develop a markedly decreased exercise tolerance and quality of life. Early PH is often asymptomatic. By the time symptoms appear, disease progression is usually well advanced. The most common symptoms of PH include shortness of breath with physical exercise (exertional dyspnea), fatigue, dizziness and fainting, all of which are worsened by exertion. PH is a severe and life-threatening disease that can lead to heart failure and death. According to the WHO classification, there are five different types of PH based on the underlying causes of PH. To date, existing treatments are indicated solely for one of these types, pulmonary arterial hypertension, which accounts for only a small portion of overall PH patients.

About Riociguat

Riociguat (BAY 63-2521) is an oral agent being investigated in phase III clinical trials as a potentially new approach to treating CTEPH and PAH, two life-threatening types of PH. Riociguat is the first member of a novel class of therapeutics called soluble guanylate cyclase (sGC) stimulators. Riociguat works through the same signaling pathway as the body's own vasodilating substance, nitric oxide (NO). NO relaxes the musculature in the blood-vessel walls, lowers the pulmonary blood pressure and relieves the heart by modulating the activity of the sGC enzyme. Riociguat has a dual mode of action: it sensitizes sGC to the body's own NO while also directly stimulating sGC independently of NO. This could be important because the NO levels in the pulmonary circulation are decreased in patients with PH. With its novel mode of action, riociguat has the potential to overcome a number of limitations of other therapies currently used to treat PH.