



Fact Sheet

Bayer Schering Pharma Development Projects
 Business Unit: Hematology/Cardiology

Development candidate BAY 63-2521 – Potential for a new treatment option in pulmonary hypertension

- Stimulation of soluble guanylate cyclase as a novel principle of action
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Status: June 2007

<p>Project description</p> <p>BAY 63-2521 is an innovative oral active substance with the potential to become a new treatment option for pulmonary hypertension. BAY 63-2521 stimulates soluble guanylate cyclase (sGC), a key enzyme in a signaling cascade with central significance in the regulation of the cardiovascular system. Preclinical and clinical data so far indicate that the sGC stimulator has a good safety profile. The results of a Phase II study in patients with pulmonary hypertension were published in June 2007. The study confirmed the therapeutic potential of BAY 63-2521 in this indication. BAY 63-2521 improved the major hemodynamic parameters to a greater extent than the comparator substance nitrogen monoxide (NO). BAY 63-2521 was well tolerated, and no serious adverse effects occurred. Phase III studies in the indication pulmonary hypertension are scheduled to start in 2008.</p>	<p>At a glance</p>
	<p>Name of the active substance</p> <p>sGC stimulator (BAY 63-2521)</p>
	<p>Type of substance</p> <p>Low molecular weight substance (small molecule)</p>
	<p>Targeted Indication</p> <p>Pulmonary hypertension</p>

<p>The medical and physiological background</p> <p>Soluble guanylate cyclase (sGC) is a key enzyme in a signaling cascade which plays a central role in the regulation of a large number of physiological processes. It is activated by the endogenously formed gas nitrogen monoxide (NO) and in its active form catalyzes the formation of cyclic guanosine monophosphate (cGMP). The neurotransmitter cGMP acts as a "second messenger", and leads, for example, to the dilatation of blood vessels, has a blood pressure-lowering effect, and mediates tissue-protective effects. Limited bioavailability of NO or reduced sensitivity to endogenous NO play a role in various diseases, e.g. cardiovascular diseases and pulmonary hypertension.</p> <p>The treatment options for pulmonary hypertension, in which the signaling pathway NO → sGC → cGMP is adversely affected or disrupted, are limited. They include the administration by inhalation of NO or substances which prevent the breakdown of cGMP (inhibitors of the enzyme phosphodiesterase), or substances which relax the blood vessels, such as prostacyclins. Direct activation of the enzyme soluble guanylate cyclase is a novel principle of action. To date, no drugs based on this principle are available.</p> <p>Pulmonary hypertension</p> <p>Pulmonary hypertension is a rare and life-threatening disorder in which the blood vessels in the lungs are constricted. This increases the blood pressure in these vessels, which overburdens the heart and may even lead to heart failure. The symptoms are non-specific, and accordingly, the disorder is frequently either not diagnosed or diagnosed too late. Pulmonary hypertension has a mortality rate similar to that of cancer. One of the established treatment options for pulmonary hypertension is the prostacyclin analogue iloprost from Bayer Schering Pharma.</p>	<p>Administration form</p> <p>Tablets</p>
	<p>Mode of action</p> <p>Stimulation of the enzyme soluble guanylate cyclase in a signaling cascade that leads to vasodilatation</p>
	<p>Status</p> <ul style="list-style-type: none"> ▪ Phase II study ongoing ▪ Phase III study planned to start in 2008

<p>Active substance</p> <p>The sGC stimulator BAY 63-2521 is a novel low molecular weight substance that acts directly on the enzyme soluble guanylate cyclase in the signaling pathway $\text{NO} \rightarrow \text{sGC} \rightarrow \text{cGMP}$ (see above). As a result of the binding of BAY 63-2521 to the enzyme sGC, the enzyme is stimulated and causes the formation of the second messenger cGMP, which can mediate the known vasodilator, blood pressure-lowering and tissue-protective effects. Preclinical studies have shown that BAY 63-2521 stimulates sGC directly and even increases the enzyme's sensitivity to NO, producing a synergistic effect.</p> <p>sGC stimulators</p> <p>sGC stimulators are substances that act directly on the enzyme soluble guanylate cyclase in the signaling pathway $\text{NO} \rightarrow \text{sGC} \rightarrow \text{cGMP}$ (see above); they activate the normally functioning enzyme and also potentiate the action of NO on the enzyme.</p>	
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Bayer HealthCare

Bayer HealthCare, a subsidiary of Bayer AG, 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, Diabetes Care and Pharmaceuticals divisions. The pharmaceuticals business operates under the name Bayer Schering Pharma and as Bayer HealthCare Pharmaceuticals in the US and Canada. Bayer HealthCare's aim is to discover and manufacture products that will improve human and animal health worldwide.

Bayer Schering Pharma

Bayer Schering Pharma is a worldwide leading specialty pharmaceutical company. Its research and business activities are focused on the following areas: Diagnostic Imaging, Hematology/Cardiology, Oncology, Primary Care, Specialized Therapeutics and Women's Healthcare. With innovative products, Bayer Schering Pharma aims for leading positions in specialized markets worldwide. Using new ideas, Bayer Schering

Pharma aims to make a contribution to medical progress and strives to improve the quality of life.

Research and Development at Bayer Schering Pharma

Bayer Schering Pharma concentrates its R&D activities on innovative treatment approaches for diseases with a high unmet medical need to improve patients' quality of life and prolong lives. In this context, Bayer Schering Pharma focuses on its core competencies and its many years of experience. Thus, Bayer Schering Pharma holds a leading position in many therapeutic fields: for example, in the treatment of hemophilia and multiple sclerosis, in contrast media and oral contraception. We are also striving for a leading position in oncology. With new approaches in cancer therapy, for cardiovascular diseases, gynaecological therapies and in molecular imaging, Bayer Schering Pharma aims to become an innovation leader in these fields. In addition, Bayer Schering Pharma further develops products already on the market in order to improve their application and/or extend their range of indications.

Contacts:

Dr. Jost Reinhard, Tel.: +49 30 468 15062

E-mail: jost.reinhard@bayerhealthcare.com

Frank Richtersmeier, Tel.: +49 30 468 17661

E-mail: frank.richtersmeier@bayerhealthcare.com

Forward-looking statements

This information contains forward-looking statements based on current assumptions and forecasts made by Bayer Group management. Various known and unknown risks, uncertainties and other factors could lead to material differences between the actual future results, financial situation, development or performance of the company and the estimates given here. These factors include those discussed in our public reports filed with the Frankfurt Stock Exchange and with the U.S. Securities and Exchange Commission (including Form 20-F). The company assumes no liability whatsoever to update these forward-looking statements or to conform them to future events or developments.