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Novartis Study Shows QTI571 Significantly Improved Walking Distance in Patients with Life-Threatening Pulmonary Arterial Hypertension

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- - Phase III IMPRES study demonstrates potential benefits of QTI571 in patients who remain symptomatic despite treatment with two or more PAH therapies(1)
- - Evidence indicates that QTI571 targets an underlying cause of PAH by counteracting uncontrolled growth of arterial smooth muscle cells(2)
- - PAH is a debilitating disease of the heart and lungs affecting up to 260,000 people worldwide(3) leading to heart failure and death(4)

EAST HANOVER, N.J., Sept. 25, 2011 /PRNewswire/ -- Novartis announced new data today from the pivotal Phase III IMPRES clinical trial showing that the investigational therapy QTI571 (imatinib) significantly improved exercise capacity in patients with pulmonary arterial hypertension (PAH) after 24 weeks compared with placebo(1). Evidence indicates that QTI571 targets an underlying cause of PAH by counteracting uncontrolled growth of arterial smooth muscle cells(2).

The IMPRES study met its primary endpoint by demonstrating a significant improvement in the six-minute walk distance (6MWD) test in patients with elevated pulmonary vascular resistance (PVR) despite treatment with two or more specific PAH vasodilator therapies(1). The 6MWD is a predictor of survival in PAH patients(5,6), and is commonly used to assess exercise capacity in PAH clinical trials(7,8,9). In the study, patients treated with QTI571 increased their mean 6MWD by 31.8 meters compared with placebo ($p=0.002$)(1).

The study's secondary endpoints showed that QTI571 produced statistically significant improvements compared to placebo in pulmonary arterial pressure, cardiac output and pulmonary vascular resistance (all $p<0.001$)(1), but not in time to clinical worsening (i.e. death, hospitalization due to PAH, worsening of functional class, or $\geq$15% drop in 6MWD) ($p=0.563$)(1).

"These results are impressive as they were achieved in patients who were already receiving two or more established PAH drugs," said Marius Hoeper MD, Associate Professor, Department of Respiratory Medicine at Hannover Medical School, Germany and principal investigator of the IMPRES study. The data were presented for the first time at the European Respiratory Society (ERS) Annual Congress in Amsterdam, The Netherlands.

PAH is a debilitating disease of the heart and lungs that is characterized by a marked and sustained elevation in pulmonary artery pressure. The disease is chronic and rapidly progressive and can result in right ventricular heart failure and death(4). An estimated 260,000 people are affected worldwide(3) and approximately half of the people diagnosed with PAH die within five years,(10).

"If approved, QTI571 has the potential to provide a further treatment option for patients where current therapies are not providing sufficient benefit in the treatment of this life-threatening disease," said David Epstein, Division Head of Novartis Pharmaceuticals. "Novartis has a strong and growing portfolio of respiratory medicines, and we are committed to expanding the support we offer to patients suffering from a number of respiratory and pulmonary disorders."

QTI571 is an oral therapy that works by inhibiting the activity of proliferative factors including platelet-derived growth factor (PDGF) which is thought to be involved, along with its receptor, in the progression of PAH(10,11). In patients with this disease, PDGF may cause smooth muscle cells in the pulmonary arteries to multiply, restricting blood flow and increasing resistance in these arteries(12).

Safety data showed that the overall incidence of adverse events was similar for QTI571 and for placebo(1). Serious adverse events and discontinuations due to serious adverse events were more frequent with QTI571(1). Adverse events were as expected for this patient population and class of drug, and were similar to those previously reported with QTI571(13).

IMPRES was a 24-week randomized placebo-controlled, double-blind, multi-center clinical trial evaluating the efficacy and safety of oral QTI571 as an add-on therapy in the treatment of patients with PAH(1). The study involved a total of 202 patients with elevated PVR of $\geq$800 dynes.sec.cm-5 despite treatment with at least two other specific PAH medications (i.e. endothelin receptor antagonists, phosphodiesterase-5 inhibitors and/or prostacyclins)(1).

Treatment was initiated at a dose of 200 mg once-daily, which was increased to 400 mg once-daily after two weeks if well tolerated. The dose could be reduced to 200 mg once-daily if treatment was not well tolerated(1).

QTI571 is currently not approved to treat PAH and is planned to be submitted for regulatory approval later this year for the treatment of this disease. Imatinib, the active ingredient in QTI571, is currently available under the trade names Glivec® and Gleevec® for use in certain oncology indications.

Disclaimer

The foregoing release contains forward-looking statements that can be identified by terminology such as "potential," "can," "estimated," "committed," "planned," or similar expressions, or by express or implied discussions regarding potential marketing approvals for QTI571 or regarding potential future revenues from QTI571. You should not place undue reliance on these statements. Such forward-looking statements reflect the current views of management regarding future events, and involve known and unknown risks, uncertainties and other factors that may cause actual results with QTI571 to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that QTI571 will be approved for sale in any market. Nor can there be any guarantee that QTI571 will achieve any particular levels of revenue in the future. In particular, management's expectations regarding QTI571 could be affected by, among other things, unexpected clinical trial results, including unexpected new clinical data and unexpected additional analysis of existing clinical data; the company's ability to obtain or maintain patent or other proprietary intellectual property protection; unexpected regulatory actions or delays or government regulation generally; competition in general; government, industry and general public pricing pressures; the impact that the foregoing factors could have on the values attributed to the Novartis Group's assets and liabilities as recorded in the Group's consolidated balance sheet, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those anticipated, believed, estimated or expected. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

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