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Novartis investigational drug ICL670 demonstrates positive results in treating chronic iron overload, a potentially life-threatening condition

- *Phase III trial in regularly transfused patients shows doses of 20 and 30 mg/kg/day to be highly effective while doses of 5 and 10 mg/kg/day not effective*
- *Treatment with ICL670 results in highly statistically significant ($p < 0.001$) absolute reduction of liver iron concentration*
- *Global submission anticipated for first half 2005 with Orphan Drug status in US and EU*

Basel, Switzerland, December 7, 2004 – The investigational drug ICL670, an oral, once-daily iron chelator, demonstrated significant efficacy at maintaining or reducing absolute liver iron concentration (LIC), an accepted indicator for total body iron content, when used at doses of 20 and 30 mg/kg/day in a Phase III trial. However, the overall trial primary endpoint of non-inferiority to deferoxamine was not met because doses of 5 and 10 mg/kg/day were not effective. Data from three studies were presented at the annual meeting of the American Society of Hematology in San Diego, California.

As a once-daily oral treatment, ICL670 is designed to be easier to use and more convenient than deferoxamine (Desferal®), the current standard iron chelation therapy, which typically requires slow infusion by pump over eight to 12 hours for at least five days a week. Additionally, ICL670 was generally well tolerated in both adults and children as young as age two years, with most adverse events being mild to moderate in severity. The ICL670 global clinical trials program is the largest ever prospectively implemented for an investigational iron chelator.

Iron overload is a cumulative, potentially life-threatening condition that may result from repeated blood transfusions required to treat certain types of anemias, including sickle cell disease, thalassemia and myelodysplastic syndromes. Over time, if left undiagnosed or untreated, iron overload can lead to debilitating and life-threatening consequences, including damage to the liver, heart and endocrine glands.

“This is a wonderful potential advancement in the treatment of chronic iron overload and could extend the benefits of chelation therapy to many patients who are not currently being treated,” said Diane Young, MD, vice president and global head of Phase II/III Clinical Development at Novartis Oncology. “Additionally, as the first once-daily oral treatment, ICL670 has the promise to free patients from the burden of daily subcutaneous infusions of therapy.”

Study Details

The international, open-label, randomized, multicenter Phase III study included 586 patients with beta-thalassemia and transfusion-related iron overload who were randomized to receive

ICL670 or deferoxamine according to a fixed dosing regimen. According to LIC at baseline, patients were randomized in a 1:1 ratio to receive either oral ICL670 once daily at doses of 5, 10, 20 or 30 mg/kg, or subcutaneous deferoxamine at doses of 20-60 mg/kg/day for 5 days/week.

The primary endpoint of the trial was the achievement of a specified reduction in liver iron concentration (LIC) after one year of therapy. Those with lower initial LIC values on the deferoxamine arm were permitted to remain on their pre-study doses and were compared to patients receiving the lower doses of 5 or 10 mg/kg/day of ICL670. Therefore, many of these individuals received significantly higher doses of deferoxamine relative to ICL670.

Because of the disproportionately low dosing of patients with ICL670 at 5 and 10 mg/kg/day when compared to deferoxamine, non-inferiority was not achieved in the overall population. Non-inferiority was demonstrated, however, in those patients treated with ICL670 at 20 and 30 mg/kg/day.

The ICL670 trial showed a highly statistically significant ($p < 0.001$) absolute reduction of LIC in the overall patient population studied. Data demonstrated that after one year of treatment, the mean overall change in LIC from baseline was -5.3 ± 8.0 mg Fe/g dry weight (dw) for patients taking doses of 20 and 30 mg/kg/day of ICL670. Patients being treated with comparable doses of deferoxamine achieved a reduction in LIC of -4.3 ± 5.8 mg Fe/g dw.

In a related, open-label Phase II trial presented at ASH, data from a study of 184 patients with myelodysplastic syndrome (MDS), other rare anemias, and patients with thalassemia unable to take deferoxamine therapy, also demonstrated maintenance or reduction of absolute LIC values in patients treated with ICL670 at doses of 20 and 30 mg/kg/day.

In these studies, ICL670 was generally well tolerated with the most frequently reported adverse events being nausea, vomiting, diarrhea, abdominal pain, skin rash and mild stable increases in serum creatinine, usually within the normal range. No unmanageable toxicities have been observed. No cases of agranulocytosis, a potentially life-threatening hematological adverse event, were reported in the ICL670 trials (more than 800 patients received ICL670). In the Phase III trial, four patients (1.4%) in the deferoxamine group and eight patients (2.7%) in the ICL670 group had discontinued therapy due to any adverse events.

Based on the positive results of these studies, Novartis anticipates submitting ICL670 in the first half of 2005 for registration with health authorities worldwide for the treatment of patients with chronic iron overload due to blood transfusions. The U.S. Food and Drug Administration granted fast-track status in 2003 for ICL670 in this patient population. A drug designated as a fast-track product is intended for the treatment of a serious or life-threatening condition and demonstrates the potential to address unmet medical needs for the condition.

Additionally, ICL670 was granted Orphan Drug status in the US and EU in 2002. In the US, the term "Orphan Drug" refers to a product that treats a disease that affects fewer than 200,000 people in the US. In the EU, the term "Orphan Drug" refers to a product that treats a serious or life-threatening disease that affects fewer than five people per 10,000 population. The intent of the Orphan Drug designation is to stimulate the research, development, and approval of products that treat rare diseases.

The foregoing release contains forward-looking statements that can be identified by terminology such as "investigational drug," "potentially," "anticipated," "designed to," "can lead," "potential advancement," "could extend," "has the promise to free," "anticipates," or similar expressions, or by discussions regarding potential regulatory approvals of ICL670, potential revenues from ICL670, or regarding the long-term impact of a patient's use of

ICL670. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results with ICL670 to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that ICL670 will be approved for any indications, or will achieve any particular level of revenues, in any market. Neither can there be any guarantee regarding the long-term impact of a patient's use of ICL670. In particular, management's ability to ensure satisfaction of the health authorities' requirements is not guaranteed and management's expectations regarding commercialization of ICL670 could be affected by, among other things, additional analysis of ICL670 clinical data; new clinical data; unexpected clinical trial results; unexpected regulatory actions or delays or government regulation generally; the company's ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; and other risks and factors referred to in the Company's current Form 20-F on file with the U.S. 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.

Additional Information

For prescribing information on Desferal please contact your local Novartis affiliate.

About Novartis

Novartis Oncology is a business unit within Novartis AG (NYSE: NVS), is a world leader in pharmaceuticals and consumer health. In 2003, the Group's businesses achieved sales of USD 24.9 billion and a net income of USD 5.0 billion. The Group invested approximately USD 3.8 billion in R&D. Headquartered in Basel, Switzerland, Novartis Group companies employ about 80,000 people and operate in over 140 countries around the world. For further information please consult <http://www.novartis.com>.

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