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MEDIA RELEASE • COMMUNIQUE AUX MEDIAS • MEDIENMITTEILUNG

Novartis receives positive CHMP opinion for Ilaris® in active Systemic Juvenile Idiopathic Arthritis, a serious form of childhood arthritis

- The CHMP has endorsed the use of Ilaris® in patients aged 2 years and older who suffer from Systemic Juvenile Idiopathic Arthritis (SJIA)

- In Phase III studies, 84% of Ilaris-treated SJIA patients achieved significant improvement of systemic and arthritic symptoms (pediatric ACR30) after a single subcutaneous dose1

- Ilaris is the first interleukin-1 beta inhibitor to receive such an opinion for the treatment of SJIA and, once approved, will be the only treatment that is given as a monthly subcutaneous injection.

Basel, July 26, 2013 – Novartis announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion for the use of Ilaris® (canakinumab) in the treatment of active systemic juvenile idiopathic arthritis (SJIA) in patients aged 2 years and older. SJIA is a rare and disabling form of childhood arthritis with limited treatment options2. The condition is characterized by spiking fever, rash and arthritis that can affect children as young as 2 years old and can continue into adulthood2,3.

This opinion was based on two Phase III trials in SJIA patients, aged 2–19, which showed significant improvement in the majority of Ilaris-treated patients1. Study 1 showed that 84% of patients treated with one subcutaneous dose of Ilaris achieved the primary endpoint of the adapted pediatric American College of Rheumatology 30 (ACR30), compared to 10% achievement of ACR30 for placebo at Day 151. In the open-label part of Study 2, 92 of 128 patients attempted “corticosteroid tapering”. Of those 92 patients, 62% were able to substantially reduce their use of corticosteroids, and 46% completely discontinued corticosteroids1. In the controlled portion of Study 2, there was a 64% relative reduction in the risk of flare for patients in the Ilaris group as compared to those in the placebo group (hazard ratio of 0.36; 95% CI: 0.17 to 0.75)1.

CHMP recommended Ilaris for the treatment of active SJIA in patients aged 2 years and older who have responded inadequately to previous therapy with non-steroidal anti-inflammatory drugs (NSAIDs) and systemic corticosteroids. CHMP stated that Ilaris can be given as monotherapy or in combination with methotrexate.

“If approved, Ilaris would provide a new treatment option for patients whose choice of therapy has, to date, been very limited,” said Timothy Wright, MD, Global Head of Development, Novartis Pharmaceuticals. “This positive opinion by the CHMP is an important step towards the approval of Ilaris for SJIA in the EU.”

The European Commission generally follows the recommendations of the CHMP and usually delivers its final decision within three months of the CHMP recommendation.
The incidence of SJIA in Europe is thought to be around 0.4–0.8 per 100 000\(^3\), with a prevalence estimated at 1–10 in 30,000 children\(^4\). Although the disease can be life-threatening, treatment options are limited. Corticosteroids are often used to treat symptoms and pain despite their long term use being associated with potentially serious adverse effects, including Cushing syndrome, growth suppression and osteoporosis\(^1\).

Ilaris is being investigated in a number of inflammatory diseases where interleukin-1 (IL-1) beta is a key component of disease pathogenesis. These include rare autoinflammatory conditions for which approved treatments do not exist, including, Tumor Necrosis Factor Receptor-Associated Periodic Syndrome (TRAPS), colchicine-resistant Familial Mediterranean Fever (FMF) and Hyper IgD Syndrome (HIDS). Ilaris is considered an investigational agent for these conditions at this point in time. As such, the role that Ilaris could play in treating these conditions and potential benefit to patients is still being determined.

**About the Pivotal Phase III Studies**

Study 1, a 4-week, randomized, double-blind, placebo-controlled study, involved 84 patients between the ages of 2 and 19 years with active SJIA\(^1,2\). Patients were treated with either a single subcutaneous dose of Ilaris (4 mg/kg, up to 300 mg) (n=43) or placebo (n=41)\(^1\). The primary endpoint was the proportion of patients achieving the adapted pediatric American College of Rheumatology (ACR) 30 response criteria and resolution of fever from baseline at Day 15\(^1\). This means that patients had at least a 30% improvement in systemic and arthritic symptoms versus baseline. The study met its primary endpoint.

Study 2, a two-part study, had an open-label, single-arm active treatment in Part I followed by a randomized, double-blind, placebo-controlled, event-driven withdrawal design in Part II\(^1\). A total of 177 patients between the ages of 2 and 19 years with active SJIA were enrolled in the study\(^1\). Some of these patients had previously participated in the Study 1. In Part I, patients received a subcutaneous dose of Ilaris (4 mg/kg, up to 300 mg) every 4 weeks\(^1\). The primary endpoint of Part I was to assess whether treatment with Ilaris allowed successful tapering of corticosteroids in at least 25% of SJIA patients who entered the study using a corticosteroid.

In Part II of the study, patients were randomized to either continue receiving Ilaris, or to receive placebo every 4 weeks (“placebo-after-Ilaris group”), until a pre-specified number (37) of flare-events (“flares”) had occurred\(^1\). The primary endpoint of Part II was to demonstrate that the time to flare was longer with Ilaris than with placebo.

The primary endpoints for Study 1 and Study 2 were all met.

**About Ilaris**

Ilaris is a selective, fully human, monoclonal antibody that inhibits IL-1 beta, which is an important part of the body’s immune system defenses\(^1\). Excessive production of IL-1 beta plays a prominent role in certain inflammatory diseases\(^5\). Ilaris works by neutralizing IL-1 beta for a sustained period of time, therefore inhibiting inflammation\(^1\).

Ilaris is approved for the treatment of SJIA in the US and for the symptomatic treatment of refractory acute gouty arthritis in the EU. Ilaris is also approved in more than 60 countries, including in the EU, US, Switzerland and Japan for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS), a rare, lifelong, genetic disorder with debilitating symptoms. The approved indication may vary depending upon the individual country.

**Disclaimer**

The foregoing release contains forward-looking statements that can be identified by terminology such as “positive opinion,” “will,” “recommended,” “expected,” “would,” generally follows,” “usually,” “is being investigated,” “investigational,” “potential,” “is still
being determined,” “could,” or similar expressions, or by express or implied discussions regarding potential new indications or labeling for Ilaris or regarding potential future revenues from Ilaris. 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 Ilaris to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Ilaris will be submitted or approved for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that Ilaris will achieve any particular levels of revenue in the future. In particular, management's expectations regarding Ilaris could be affected by, among other things, unexpected regulatory actions or delays or government regulation generally; unexpected clinical trial results, including unexpected new clinical data and unexpected additional analysis of existing clinical data; government, industry and general public pricing pressures; competition in general; the company's ability to obtain or maintain patent or other proprietary intellectual property protection; unexpected manufacturing issues; 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.

About Novartis
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