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Novartis biological drug Ilaris[®] approved in EU to treat children and adults with CAPS, a rare debilitating auto-inflammatory disease

- *First drug approved in EU for patients as young as four years old with cryopyrin-associated periodic syndrome (CAPS)¹*
- *Approval based on positive data showing Ilaris produced rapid and sustained remission of CAPS symptoms in up to 97% of patients²*
- *Ilaris is a monoclonal antibody that selectively targets and blocks interleukin-1 beta (IL-1 β), the trigger for inflammation and tissue damage in CAPS patients^{1,2,3}*
- *Studies ongoing in groups of patients with other diseases involving IL-1 β such as COPD, type 2 diabetes and gout – one of the most painful forms of arthritis*

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Basel, October 28, 2009 – The new biological medicine Ilaris[®] (canakinumab) has been approved in the European Union (EU) to treat adults and children as young as four years old with cryopyrin-associated periodic syndrome (CAPS), a rare life-long auto-inflammatory disease with debilitating symptoms and few treatment options^{1,2,3}.

The accelerated EU decision follows approvals in the US and Switzerland, where Ilaris was granted priority review in view of the significant unmet medical need. Ilaris is the only medicine approved in the EU for CAPS patients as young as four years old, and for patients with the most debilitating form of CAPS, neonatal-onset multisystem inflammatory disease (NOMID)⁴. It is a fully human monoclonal antibody given by injection under the skin once every two months – the longest dosing interval of any available treatment^{2,5,6}.

“We are excited by the latest approval because Ilaris represents a significant therapeutic advance for patients with this debilitating and sometimes fatal disease,” said Joe Jimenez, CEO of the Novartis Pharmaceuticals Division. “Ilaris is the outcome of our pathways-driven search for innovative medicines that are tailored to the needs of patients. Initially we studied Ilaris in a very rare disease with a well-understood genetic profile, and now that its efficacy has been proven, we are able to move ahead rapidly with development in other diseases characterized by the same inflammatory process.”

The regulatory submission was supported by data showing that Ilaris produced rapid and sustained remission of symptoms in up to 97% of CAPS patients, with most of them responding within hours of the first injection².

Ilaris, previously known as ACZ885, targets and normalizes the production of a protein within the immune system called interleukin-1 beta (IL-1 β)^{1,3,7}. In CAPS patients, IL-1 β is overproduced causing widespread inflammation and tissue damage^{3,8,9}. Symptoms, such as debilitating fatigue, fever, joint pain and conjunctivitis, can be present from infancy and continue throughout the patient’s life^{2,3}.

If left untreated, CAPS may have serious consequences such as deafness, bone deformities, erosive joint destruction, and central nervous system damage leading to loss of vision^{1,2,3}. Around 25% of patients develop amyloidosis, a condition in which the build-up of proteins can cause vital organs to fail, resulting in renal failure and requiring kidney transplantation. Approximately 20% of patients with NOMID, the most severe form of CAPS, die before reaching adulthood^{2,3,10}.

CAPS is believed to occur in around one in 2,500 people in the EU^{3,11}, but fewer than 1,000 cases have been reported worldwide due to poor diagnosis^{1,3}. CAPS includes three distinct autoinflammatory disorders of increasing severity: familial cold auto-inflammatory syndrome (FCAS), Muckle-Wells syndrome (MWS), and NOMID^{2,3}. Ilaris is the only treatment indicated in the EU and Switzerland to treat all three disorders^{1,4}.

Studies with ACZ885 are ongoing in other diseases in which IL-1 β plays an important role, such as chronic obstructive pulmonary disease (COPD), type 2 diabetes, systemic juvenile idiopathic arthritis (SJIA), and gout – one of the most painful forms of arthritis. Not all potential patients with these diseases would be eligible for treatment with ACZ885, if approved.

The CAPS filing was based on a clinical trial program involving more than 100 patients. Data from a pivotal study published in *The New England Journal of Medicine* show that Ilaris produced a rapid, complete and sustained response in most patients². None of the patients treated with Ilaris (0 out of 15) experienced a disease outbreak or ‘flare’ compared to 13 of the 16 patients who received placebo (0% vs. 81% respectively, $p < 0.001$)².

“In CAPS studies, symptoms improved within 24 hours after patients received a single dose of Ilaris. The disease was barely detectable in the blood after two weeks and the remission of symptoms was sustained for six months,” said Helen J. Lachmann, MD of the UK National Amyloidosis Centre at the Royal Free and University College Medical School in London, UK. “By effectively turning off the disease activity, Ilaris has the potential to transform patients’ lives by offering long-term control of their disease.”

Ilaris was generally well tolerated and there was no consistent pattern of adverse events apart from a slight increase in infections². Two patients experienced serious adverse events, namely a lower urinary tract infection and vertigo². The most common adverse events were nasopharyngitis, diarrhea, influenza, headache and nausea². Ilaris was not associated with any severe injection-site reactions and those that did occur were classified as mild-to-moderate².

The EU approval was granted under exceptional circumstances, a common practice with so-called orphan drugs. This reflects a need for additional data due to factors such as the rarity of the disease or lack of scientific knowledge. The situation is reviewed every year until the European Medicines Agency (EMA) is able to grant a normal approval.

In addition to its orphan drug status for CAPS, Ilaris has been designated as an orphan drug for treating SJIA, the most severe form of arthritis in children, in the US, EU and Switzerland, and has fast-track status for SJIA in the US. Orphan drugs are those developed to treat diseases affecting fewer than 200,000 people (in the US)¹² or fewer than five out of 10,000 people (in the EU)¹³.

Ilaris was approved in Switzerland in July 2009 to treat all three forms of CAPS in adults and children over four years old, and in the US in June 2009 to treat two forms of CAPS, namely FCAS and MWS, while a study in NOMID patients is under way. Priority reviews are ongoing in other countries including Australia, Brazil and Canada.

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References

1. National Horizon Scanning Centre. Canakinumab for cryopyrin associated periodic syndrome. November 2008. Available at: <http://www.pcpoh.bham.ac.uk/publichealth/horizon/outputs/documents/2008/sept-dec/Canakinumab.pdf> Last accessed September 23, 2009.
2. Lachmann HJ, Kone-Paut I, Kuemmerle-Deschner JB, *et al.* Use of Canakinumab in the Cryopyrin-Associated Periodic Syndrome. *N Engl J Med* 2009; 360: 2416 - 2425
3. Durrant KLW, Goldbach-Mansky R, Hoffman H, Leslie K, Rubin B. CAPS Cryopyrin-Associated Periodic Syndromes 2008. Available at: <http://www.nomidalliance.net/Download1.html>. Last accessed September 23, 2009.
4. Ilaris (canakinumab) prescribing information.
5. Arcalyst (rilonacept) prescribing information.
6. Kineret (anakinra) prescribing information.
7. Kastner DL. Hereditary Periodic Fever Syndromes. Hematology 2005 – American Society of Hematology Education Program. 2005: 74-81. Available at: <http://asheducationbook.hematologylibrary.org/cgi/reprint/2005/1/74>
8. Joost PH, Drenth MD, Jos W.M. van der Meer. The Inflammasome – A Linebacker of Innate Defense. *N Engl J Med* 2006 355(7): 730-732.
9. Lachmann HJ, Lowe P, Felix SD, *et al.* In vivo regulation of interleukin 1 in patients with cryopyrin-associated periodic syndromes. *J Exp Med* 2009. Published online April 13, 2009. Available at: www.jem.org/cgi/doi/10.1084/jem.20082481.

10. Prieur A-M. CINCA syndrome. October 2003. Orphanet. Available at: <http://www.orpha.net/data/patho/Pro/en/CINCA-FRenPro3395.pdf> Last accessed September 23, 2009.
11. European Medicines Agency (EMA). Pre-authorisation evaluation of medicines for human use. Committee for orphan medicinal products. Available at: <http://www.emea.europa.eu/pdfs/human/comp/opnion/17086808en.pdf>. Last accessed September 23, 2009.
12. Orphan Drug Act. US Food and Drug Administration. Section 526 (2), Line 2.
13. The orphan drug strategy. Europa: Gateway to the European Union. Paragraph 1, Line 1.

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Novartis Media Relations

Eric Althoff

Novartis Global Media Relations
+41 61 324 7999 (direct)
+41 79 593 4202 (mobile)
eric.althoff@novartis.com

Irina Ferluga

Novartis Pharma Communications
+41 61 324 2422 (direct)
+41 79 824 1121 (mobile)
irina.ferluga@novartis.com

e-mail: media.relations@novartis.com

Novartis Investor Relations

Central phone: +41 61 324 7944
Ruth Metzler-Arnold +41 61 324 9980
Pierre-Michel Bringer +41 61 324 1065
John Gilardi +41 61 324 3018
Thomas Hungerbuehler +41 61 324 8425
Isabella Zinck +41 61 324 7188

North America:

Richard Jarvis +1 212 830 2433
Jill Pozarek +1 212 830 2445
Edwin Valeriano +1 212 830 2456

e-mail: investor.relations@novartis.com

e-mail: investor.relations@novartis.com