

**MEDIA RELEASE • COMMUNIQUE AUX MEDIAS • MEDIENMITTEILUNG****Ilaris<sup>®</sup> recommended for European approval as new biologic drug to treat a rare but serious group of auto-inflammatory diseases**

- *Set to become first medicine in EU to treat patients aged four and older suffering from life-long cryopyrin-associated periodic syndrome (CAPS)<sup>1</sup>*
- *Ilaris targets interleukin-1 beta (IL-1 $\beta$ ), a key driver of inflammation<sup>1,2,3</sup> – studies ongoing in other diseases involving IL-1 $\beta$  such as gout, COPD and type 2 diabetes*
- *EU opinion follows US and Swiss approvals based on data showing Ilaris produced rapid and sustained remission in CAPS patients after one dose<sup>2</sup>*
- *CAPS comprises three disorders of increasing severity with potentially fatal complications<sup>2,3</sup> – most patients suffer from severe and disabling symptoms<sup>1,3</sup>*

**Basel, July 24, 2009** – The biotechnology medicine Ilaris<sup>®</sup> (canakinumab) has passed another major milestone with a recommendation for approval in the European Union to treat patients with a life-long and potentially fatal auto-inflammatory disease called cryopyrin-associated periodic syndrome (CAPS). When approved, Ilaris will be the only treatment in the EU indicated for CAPS patients aged four years and older<sup>1</sup>.

Ilaris represents an important advance in the development of personalized medicines because it targets a condition that is triggered by a specific genetic mutation. In CAPS patients, this mutation drives the overproduction of interleukin 1-beta (IL-1 $\beta$ ) which causes the widespread sustained inflammation and tissue damage associated with the disease<sup>3,4,5</sup>.

Because Ilaris normalizes the production of IL-1 $\beta$ <sup>1,2,3</sup>, it is also being studied in other diseases in which IL-1 $\beta$  plays a pivotal role such as systemic juvenile idiopathic arthritis (SJIA), gout, chronic obstructive pulmonary disorder (COPD), and type 2 diabetes.

“By concentrating initially on a rare syndrome with a well-defined disease process such as CAPS, we have been able to demonstrate a clear therapeutic advantage with Ilaris,” said Trevor Mundel, MD, Head of Global Development at Novartis Pharma AG. “Our focus now is to establish whether this could also provide a new approach to the treatment of other diseases involving a similar underlying process.”

A positive opinion recommending the approval of Ilaris for CAPS was issued by the Committee for Medicinal Products for Human Use (CHMP), which reviews medicines for the European Commission. The recommendation comes shortly after approvals in the US and Switzerland where Ilaris was granted priority review based on its potential to fulfil an important unmet need for CAPS patients.

The EU submission was supported by data showing that Ilaris, a monoclonal antibody formerly known as ACZ885, produced rapid and sustained remission of symptoms in up to 97% of CAPS patients, with most responding from the first injection<sup>2</sup>.

Ilaris is given by subcutaneous injection only once every two months making it a convenient treatment, especially for younger patients<sup>2</sup>. More than 90% of patients studied were free from painful injection-site reactions<sup>2</sup>.

CAPS includes three distinct auto-inflammatory disorders. These are familial cold auto-inflammatory syndrome (FCAS) which is the mildest form of CAPS, Muckle-Wells syndrome (MWS), and neonatal-onset multisystem inflammatory disease (NOMID, also known as chronic infantile neurological cutaneous articular syndrome or CINCA) – the most severe form of the disease<sup>2,3</sup>.

“CAPS is a life-long and potentially fatal condition for which there are currently no approved medications in the European Union,” said Helen J. Lachmann, MD of the UK National Amyloidosis Centre at UCL Medical School in London, UK. “In clinical trials, canakinumab has been shown to switch off disease activity in as little as 24 hours following a single dose. It has the potential to transform patients’ lives, not only providing relief from their debilitating daily symptoms but also offering the possibility of long-term control of the disease.”

The symptoms of CAPS, such as debilitating fatigue, rash, fever, headaches, joint pain and conjunctivitis, can be present from birth or infancy, and can occur daily throughout patients’ lives<sup>2,3</sup>. Serious long-term consequences may include deafness, bone deformities, erosive joint destruction, and central nervous system damage leading to loss of vision<sup>1,2,3</sup>. Around 25% of CAPS patients develop amyloidosis, a condition in which the build-up of proteins can cause vital organs to fail, resulting in renal failure and death within five to 10 years<sup>1</sup>.

CAPS is believed to occur in around 6,500 patients worldwide and 2,500 in the EU<sup>3,6</sup>. However due to lack of diagnosis or misdiagnosis, fewer than 1,000 cases have been officially reported worldwide<sup>1,3</sup>.

The Ilaris filing was based on a clinical trial program involving more than 100 CAPS patients. The pivotal study is a three-part, one-year Phase III study involving 35 patients aged nine to 74 years old with varying degrees of disease severity<sup>2</sup>. Data published in *The New England Journal of Medicine* in June 2009 show that Ilaris produced a rapid, complete and sustained response in the majority of patients<sup>2</sup>.

Results for the primary endpoint showed that 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,  $p < 0.001$ )<sup>2</sup>.

In general, Ilaris was well tolerated with no consistent pattern of adverse events apart from a slight increase in infections<sup>2</sup>. Two patients experienced serious adverse events, namely a lower urinary tract infection and vertigo<sup>2</sup>. The most common adverse events reported in Ilaris-treated patients were nasopharyngitis, diarrhea, influenza, headache and nausea<sup>2</sup>.

No impact on the type or frequency of adverse events was seen with longer-term treatment<sup>2</sup>. Ilaris was not associated with any severe reactions at the injection site, and those that did occur were mild-to-moderate in nature<sup>2</sup>.

The CHMP recommended approval under exceptional circumstances, granted when comprehensive data are not yet available due to the rarity of the disease or limited scientific knowledge. The approval is subject to certain obligations for the company and is re-assessed each year until normal approval can be given.

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. A study in NOMID patients is under way in the US and priority reviews are being conducted in other countries, including Australia and Canada.

In addition to orphan drug status for CAPS, Ilaris has also been designated as an orphan drug for treating systemic juvenile idiopathic arthritis (SJIA) 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)<sup>7</sup> or fewer than five out of 10,000 people (in the EU)<sup>8</sup>.

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