

Novartis receives three FDA Breakthrough Therapy Designations for Ilaris to treat rare types of Periodic Fever Syndromes

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- -- Subject to approvals, Ilaris® (canakinumab) will likely be first FDA-approved treatment for TRAPS and HIDS/MKD, and an important alternative treatment for patients with FMF
- -- Designations support potential expedited review of Ilaris to help address the unmet need of patients with these rare conditions
- -- Ilaris is an effective and well-tolerated treatment already approved in the US for two other autoinflammatory conditions; Systemic Juvenile Idiopathic Arthritis and two subtypes of Cryopyrin-Associated Periodic Syndromes

EAST HANOVER, N.J., April 27, 2016 /PRNewswire/ -- Novartis today announced that the US Food and Drug Administration (FDA) has granted three Breakthrough Therapy Designations for Ilaris® (canakinumab) to treat three rare types of Periodic Fever Syndromes, also known as Hereditary Periodic Fevers¹. This means Novartis will work closely with the FDA to expedite the regulatory review of Ilaris for these conditions.

Periodic Fever Syndromes are a group of autoinflammatory diseases that cause disabling and recurrent fevers, which may be accompanied by joint pain and swelling, muscle pain and skin rashes, with complications that can be life-threatening². Most patients present with symptoms in infancy or childhood³. The three conditions for which Ilaris is being reviewed are Tumor Necrosis Factor-Receptor Associated Periodic Syndrome (TRAPS) and Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD), and in Familial Mediterranean Fever (FMF) patients who are not adequately controlled with colchicine¹.

"This is an important day for patients, including many children, who are affected by these serious and debilitating syndromes that have no or limited treatment options," said David Epstein, Division Head, Novartis Pharmaceuticals. "Ilaris is a promising medicine under review for these conditions, marking our commitment to making a significant difference to the lives of people with rare diseases."

The FDA considers a treatment a Breakthrough Therapy if it is intended to treat a serious or life-threatening condition and preliminary evidence indicates it may be better than existing treatments. If approved, Ilaris will likely be the first medicine to gain approval from drug regulators for the treatment of TRAPS and HIDS/MKD, and it will be an alternative to the only FDA-approved treatment for FMF, colchicine.

The Breakthrough Therapy Designations were granted based on the pivotal Phase III trial ("Canakinumab Pivotal Umbrella Study in Three Hereditary Periodic Fevers")⁴. Based on this study Novartis submitted three supplemental Biologic License Applications in the US to register Ilaris for use in these indications.

Ilaris was approved by the FDA in 2009 to treat two subtypes of a rare autoinflammatory disease called Cryopyrin-Associated Periodic Syndromes (CAPS): Muckle-Wells syndrome (MWS) and Familial Cold Autoinflammatory Syndrome (FCAS), in patients aged four and older. In 2013, the FDA approved Ilaris for a rare, autoinflammatory form of juvenile idiopathic arthritis called Systemic Juvenile Idiopathic Arthritis (SJIA) in

patients aged two and older.

About Periodic Fever Syndromes

Periodic Fever Syndromes are a group of autoinflammatory diseases that cause serious recurrent fevers that do not have an infectious cause. Most patients present with symptoms in infancy or childhood, but in some patients the condition only becomes apparent or diagnosed in adulthood^{2,3}.

There are no approved medicines available to treat TRAPS or HIDS/MKD and very limited options for patients with FMF. Current treatments, such as oral anti-inflammatory drugs, for example corticosteroids, only help manage the symptoms. While medicines such as non-steroidal anti-inflammatory drugs (NSAIDs), have some effect at reducing symptoms, they do not prevent or change the course of an episode of fever².

Of the three rare conditions for which Ilaris is being reviewed by the FDA, FMF is the most common and mainly affects people of Eastern Mediterranean ancestry, affecting 1 in 250 to 1 in 1,000 individuals in these populations. It is far less common in other ethnic groups, but it can affect anyone³. TRAPS and HIDS/MKD are less common, with only about 1-2 people per million affected³.

About Ilaris

Ilaris (canakinumab) is a selective, high-affinity, and human monoclonal antibody that inhibits Interleukin-1 (IL-1) beta, which is an important part of the body's immune system defenses⁵. Excessive production of IL-1 beta plays a prominent role in certain inflammatory diseases^{6,7}. Ilaris works by blocking the action of IL-1 beta for a sustained period of time, therefore, inhibiting inflammation⁵ that is caused by its over-production⁵.

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 70 countries, including in the EU, Switzerland, Canada, and Japan for the treatment of CAPS, rare, lifelong, genetic disorders with debilitating symptoms. In the US, Ilaris is approved for two subtypes of CAPS: MWS and FCAS. The approved indications may vary depending upon the individual country.

IMPORTANT SAFETY INFORMATION

ILARIS can cause serious side effects, including increased risk of serious infections. ILARIS can lower the ability of your immune system to fight infections. Your health care provider should test you for tuberculosis (TB) before you receive ILARIS, monitor you closely for symptoms of TB during treatment with ILARIS, and check you for symptoms of any type of infection before, during, and after treatment with ILARIS. Tell your health care provider right away if you have any symptoms of an infection such as fever, sweats or chills, cough, flu-like symptoms, weight loss, shortness of breath, blood in your phlegm, sores on your body, warm or painful areas on your body, diarrhea or stomach pain, or feeling very tired.

You should not receive ILARIS if you are allergic to canakinumab or any of the ingredients in ILARIS.

Before receiving ILARIS, tell your health care provider about all your medical conditions, including if you have or are being treated for an active infection, have symptoms of infection, have a history of infections that keep coming back, have a history of low white blood cells, have or have had HIV, Hepatitis B, or Hepatitis C, are scheduled to receive any immunizations (vaccines). You should not get live vaccines if you are receiving ILARIS.

Patients should tell their health care provider if they are pregnant or planning to become pregnant. It is not known if ILARIS will harm an unborn baby. Patients who become pregnant while receiving ILARIS should tell their health care provider right away. Breastfeeding is not recommended during ILARIS therapy.

Tell your health care provider about all the medicines you take, including prescription and nonprescription medicines, vitamins, and herbal supplements. Especially tell your health care provider if you take medicines that affect the immune system, medicines called interleukin-1 (IL-1) blocking agents such as Kineret[®] (anakinra) or Arcalyst[®] (rilonacept), medicines called Tumor Necrosis Factor (TNF) inhibitors such as Enbrel[®] (etanercept), Humira[®] (adalimumab), Remicade[®] (infliximab), Simponi[®] (golimumab), or Cimzia[®] (certolizumab pegol), medicines that affect enzyme metabolism. Ask your health care provider if you are not sure.

ILARIS can cause serious side effects including serious infections; decreased ability of the body to fight infections (immunosuppression). For people treated with medicines that cause immunosuppression like ILARIS, the chances of getting cancer may increase; allergic reactions. Allergic reactions can happen while receiving ILARIS. Call your health care provider right away if you have any of these symptoms of an allergic reaction: rash, itching and hives, difficulty breathing or swallowing, dizziness, or feeling faint; risk of infection with live vaccines. You should not get live vaccines if you are receiving ILARIS. Tell your health care provider if you are scheduled to receive any vaccines.

The most common side effects of ILARIS when used for the treatment of CAPS include: cold symptoms, diarrhea, flu (influenza), runny nose, nausea, headache, cough, weight gain, feeling like you are spinning (vertigo), and injection site reactions (eg, redness, swelling, warmth, itching)

The most common side effects of ILARIS when used for the treatment of SJIA include: cold symptoms, upper respiratory tract infection, pneumonia, runny nose, sore throat, urinary tract infection, nausea, vomiting and diarrhea (gastroenteritis), stomach pain, and injection site reactions (eg, redness, swelling, warmth, itching)

Tell your health care provider about any side effect that bothers you or does not go away.

What is Macrophage Activation Syndrome (MAS)?

MAS is a syndrome associated with SJIA that can lead to death. Tell your health care provider right away if your SJIA symptoms get worse or if you have any of these symptoms of an infection:

- a fever lasting longer than 3 days
- a cough that does not go away
- redness in one part of your body
- warm feeling or swelling of your skin

Disclaimer

The foregoing release contains forward-looking statements that can be identified by words such as "Breakthrough Therapy," "pending," "will," "potential," "may," "can," "being reviewed," "promising," "under review," "commitment," or similar terms, 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 are based on the current beliefs and expectations of management regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking 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 be commercially successful 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; the uncertainties inherent in research and development, including unexpected clinical trial results and additional analysis of existing clinical data; the company's ability to obtain or maintain proprietary intellectual

property protection; general economic and industry conditions; global trends toward health care cost containment, including ongoing pricing pressures; unexpected safety issues; unexpected manufacturing or quality issues, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. 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

Located in East Hanover, New Jersey, Novartis Pharmaceuticals Corporation is an affiliate of Novartis AG, which provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, eye care and cost-saving generic pharmaceuticals. Novartis is the only global company with leading positions in these areas. In 2015, the Group achieved net sales of USD 49.4 billion, while R&D throughout the Group amounted to approximately USD 8.9 billion (USD 8.7 billion excluding impairment and amortization charges). Novartis Group companies employ approximately 118,000 full-time-equivalent associates. Novartis products are available in more than 180 countries around the world. For more information, please visit <http://www.novartis.com>.

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