Novartis initiates study evaluating impact of higher dosing of Cosentyx® in patients with ankylosing spondylitis

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- - ASLeap trial to evaluate impact of increasing the dose of Cosentyx (secukinumab) to 300 mg in patients who do not achieve symptom remission after 16 weeks of treatment with the approved dose of 150 mg
- - Additional exploratory analysis to investigate sleep disturbance, fatigue and daytime activity, some of the most common concerns for patients with ankylosing spondylitis(1, 2)
- - Enrollment expected to begin January 2018(1)

EAST HANOVER, N.J., Dec. 7, 2017 /PRNewswire/ -- Novartis announced today the initiation of the ASLeap trial in patients with ankylosing spondylitis (AS), evaluating the effect of changing to a higher dose (300 mg) of Cosentyx® (secukinumab) in patients who do not achieve symptom remission after treatment with Cosentyx 150 mg for 16 weeks. The primary endpoint of ASLeap is to determine the difference between Cosentyx 300 mg and Cosentyx 150 mg at Week 52 based on the proportion of subjects achieving inactive disease status based on the Ankylosing Spondylitis Disease Activity Score (ASDAS).[1]

"An important goal of ankylosing spondylitis treatment is to provide as much symptom relief as possible for patients living with this debilitating disease," said Marcia Kayath, Head US Clinical Development and Medical Affairs, Novartis Pharmaceuticals Corporation. "While Cosentyx 150 mg has shown clinically significant results in treating a majority of patients with AS, we want to investigate whether some patients may benefit from a higher dose. We hope that the results of the ASLeap study will help provide physicians with important information about how best to manage these patients."

An exploratory analysis will also assess sleep disturbance and daytime activity in patients with AS, as measured by the use of a wearable motion biosensor, an Actiwatch®* device, which is a medical device resembling a wristwatch used to collect detailed information on sleep and physical activity. Patients with AS report chronic and extensive sleep disturbance due to pain and stiffness during the night.[2] In AS patients, poor quality sleep is strongly correlated with increased pain, fatigue, lower quality of life, higher depressed mood, higher disease activity and reduced physical function.[3]

The study is expected to begin enrollment in January 2018 and aims to enroll approximately 270 patients at 70 centers in the United States. More information can be found at www.clinicaltrials.gov.

About the ASLeap Study
The ASLeap study design includes an initial 16 week open-label period (Treatment Period 1), followed by a randomized, double-blind, parallel-group period (Treatment Period 2). During the initial 16 weeks of the trial, all patients will receive open-label 150 mg Cosentyx. At Week 16, based on whether patients have met the definition of ASDAS inactive disease, patients will be placed into one of the following three groups for the remaining 36 weeks of the trial: Responders, patients who achieve ASDAS inactive disease (total score <1.3) at both Week 12 and Week 16, will enter Treatment Period 2 and continue receiving blinded Cosentyx 150 mg through Week 48. Inadequate Responders, patients who are not in inactive disease status, defined as an

ASDAS total score of ≥1.3, at both Week 12 and Week 16, will enter Treatment Period 2 and be randomized (1:1, double-blinded) to Cosentyx 300 mg or Cosentyx 150 mg through Week 48. Non-responders, patients who exhibit no change or an increase (worsening) from baseline in total ASDAS score at either Week 12 or Week 16, will complete the study at Week 16.

The study population will consist of male and female patients, ≥18 years of age with a clinical diagnosis of moderate to severe AS fulfilling the Modified New York criteria for AS despite previous or current NSAIDs/non-biologic DMARDs and/or anti-TNFα therapy. Patients must have active AS, as measured by the following: total BASDAI ≥4 on a scale of 0-10 at baseline, spinal pain as measured by BASDAI question #2 ≥4 on a scale of 0-10 at baseline, and total back pain as measured by visual analog scale (VAS) ≥40mm (0-100 mm) at baseline. [1]

About ankylosing spondylitis (AS)
Ankylosing spondylitis (AS) is a painful and often progressively debilitating disease, caused by spine inflammation that can result in irreversible damage.[4] Up to 70% of patients who go on to develop severe AS will form spinal fusions (where the bones grow together) over 10 to 15 years, which significantly reduces mobility.[5] People in their teens and twenties, particularly males, are affected most often. Family members of those with AS are at higher risk.[4,6] Approximately 20-40% of patients do not respond well to standard of care biologic medicines, and there have been few therapeutic options for those people.[7]

About Cosentyx (secukinumab) and interleukin-17A (IL-17A)
Cosentyx is a fully human monoclonal antibody (mAB) that selectively binds to the interleukin-17A (IL-17A) cytokine and inhibits its interaction with the IL-17 receptor.[8,9]

Cosentyx is the only IL-17a antagonist approved for the treatment of adults with active ankylosing spondylitis. Cosentyx is approved in more than 70 countries, which includes the European Union countries and the US. Cosentyx is also approved for the treatment of PsA and pustular psoriasis in Japan.[10]

In addition, Cosentyx is approved in more than 75 countries for the treatment of moderate to severe plaque psoriasis, which includes the European Union countries, Japan, Switzerland, Australia, the US and Canada. In Europe, Cosentyx is approved for the first-line systemic treatment of moderate to severe plaque psoriasis in adult patients.[11] In the US, Cosentyx is approved as a treatment for moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy (light therapy).[9]

To date, more than 100,000 patients worldwide have been prescribed Cosentyx in the post-marketing setting across all indications.[12] In addition, 2017 marks 10 years since the first patient visit in a clinical trial with Cosentyx.[12]

INDICATIONS

Cosentyx is a human interleukin-17A antagonist indicated for the treatment of:

- moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy
- adults with active psoriatic arthritis (PsA)
- adults with active ankylosing spondylitis (AS)

The approved dosage for the treatment of AS is 150 mg.

IMPORTANT SAFETY INFORMATION

Do not use Cosentyx if you have had a severe allergic reaction to secukinumab or any of the other ingredients in Cosentyx. See the Medication Guide for a complete list of ingredients.

Cosentyx is a medicine that affects your immune system. Cosentyx may increase your risk of having serious side effects such as:

Infections

Cosentyx may lower the ability of your immune system to fight infections and may increase your risk of infections.

- Your doctor should check you for tuberculosis (TB) before starting treatment with Cosentyx.
- If your doctor feels that you are at risk for TB, you may be treated with medicine for TB before you begin treatment with Cosentyx and during treatment with Cosentyx.
- Your doctor should watch you closely for signs and symptoms of TB during treatment with Cosentyx. Do not take Cosentyx if you have an active TB infection.

Before starting Cosentyx, tell your doctor if you:

- are being treated for an infection
- have an infection that does not go away or that keeps coming back
- have TB or have been in close contact with someone with TB
- think you have an infection or have symptoms of an infection such as:

- fevers, sweats, or chills
- muscle aches
- cough
- shortness of breath
- blood in your phlegm
- weight loss
- warm, red, or painful skin or sores on your body
- diarrhea or stomach pain
- burning when you urinate or urinate more often than normal

After starting Cosentyx, call your doctor right away if you have any signs of infection listed above. Do not use Cosentyx if you have any signs of infection unless you are instructed to by your doctor.

Inflammatory Bowel Disease

New cases of inflammatory bowel disease or "flare-ups" can happen with Cosentyx, and can sometimes be serious. If you have inflammatory bowel disease (ulcerative colitis or Crohn's disease), tell your doctor if you have worsening disease symptoms during treatment with Cosentyx or develop new symptoms of stomach pain or diarrhea.

Serious Allergic Reactions

Serious allergic reactions can occur. Get emergency medical help right away if you get any of the following symptoms: feeling faint; swelling of your face, eyelids, lips, mouth, tongue, or throat; trouble breathing or throat tightness; chest tightness; or skin rash. If you have a severe allergic reaction, do not give another injection of Cosentyx.

Before starting Cosentyx, tell your doctor if you:

- have any of the conditions or symptoms listed above for infections
- have inflammatory bowel disease (Crohn's disease or ulcerative colitis)
- are allergic to latex. The needle caps contain latex.
- have recently received or are scheduled to receive an immunization (vaccine). People who take Cosentyx should not receive live vaccines.
- have any other medical conditions
- are pregnant or plan to become pregnant. It is not known if Cosentyx can harm your unborn baby. You and your doctor should decide if you will use Cosentyx.
- are breastfeeding or plan to breastfeed. It is not known if Cosentyx passes into your breast milk.

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Know the medicines you take. Keep a list of your medicines to show your doctor and pharmacist when you get a new medicine.

How should I use Cosentyx?

See the detailed Instructions for Use that comes with your Cosentyx for information on how to prepare and inject a dose of Cosentyx, and how to properly throw away (dispose of) used Cosentyx Sensoready® pens and prefilled syringes.

- Use Cosentyx exactly as prescribed by your doctor.
- If your doctor decides that you or a caregiver may give your injections of Cosentyx at home, you should receive training on the right way to prepare and inject Cosentyx. Do not try to inject Cosentyx yourself, until you or your caregiver has been shown how to inject Cosentyx by your doctor or nurse.

The most common side effects of Cosentyx include: cold symptoms, diarrhea, and upper respiratory infections. These are not all of the possible side effects of Cosentyx. Call your doctor for medical advice about side effects.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please see accompanying full Prescribing Information, including Medication Guide.

Disclaimer
This press release contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements can generally be identified by words such as "potential," "can," "will," "plan," "expect," "anticipate," "look forward," "believe," "committed," "investigational," "pipeline," "launch," or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for the investigational or approved products described in this press release, or regarding potential future revenues from such products. You should not place undue reliance on these statements. Such forward-looking statements are based on our current beliefs and expectations regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one

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About Novartis
Located in East Hanover, NJ Novartis Pharmaceuticals Corporation is an affiliate of Novartis 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, cost-saving generic and biosimilar pharmaceuticals and eye care. Novartis has leading positions globally in each of these areas. In 2016, the Group achieved net sales of USD 48.5 billion, while R&D throughout the Group amounted to approximately USD 9.0 billion. Novartis Group companies employ approximately 121,000 full-time-equivalent associates. Novartis products are sold in approximately 155 countries around the world. For more information, please visit http://www.novartis.com.

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* Actiwatch® is a registered trademark of Mini-Mitter Co. Inc.

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