Novartis announces publication of two landmark studies in NEJM demonstrating efficacy of Cosentyx® in patients with ankylosing spondylitis

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- - Cosentyx (secukinumab) is the first IL-17A antagonist to complete Phase III studies which demonstrated efficacy and assessed safety in ankylosing spondylitis (AS)(1)
- - Cosentyx provided improvements in the signs and symptoms, physical function and quality of life measures in active AS(1)
- - Exploratory analyses showed improvements in AS signs and symptoms with Cosentyx at Week 1 and responses were sustained from Week 16 primary endpoint through to Week 52(1)
- - AS is a painful and often progressively debilitating disease, caused by spine inflammation that can result in irreversible structural damage reducing patients' mobility and quality of life(2)

EAST HANOVER, N.J., Dec. 23, 2015 /PRNewswire/ -- Novartis announced today that the results of the MEASURE 1 and MEASURE 2 Phase III studies for Cosentyx® (secukinumab) in ankylosing spondylitis (AS) were published in The New England Journal of Medicine (NEJM). These pivotal studies demonstrated significant clinical improvements with Cosentyx versus placebo in reducing the signs and symptoms of active AS – a long-term, painful and debilitating inflammation of the spine.[1,2]

In both studies, the primary endpoint was the proportion of patients meeting the Assessment of Spondyloarthritis International Society 20 (ASAS20) response criteria at Week 16 with Cosentyx 150 mg. In MEASURE 1 and MEASURE 2, ASAS20 response rates with Cosentyx 150 mg vs placebo at Week 16 were 61% (vs 29%, $p<0.001$) and 61% (vs 28%, $p<0.001$), respectively. Patients enrolled in these studies were either inadequate responders or intolerant to anti-tumor-necrosis-factor medicines (anti-TNFs), or had not been previously treated with anti-TNF therapies.[1]

In exploratory analyses, clinical improvements with Cosentyx were seen at Week 1 and ASAS20 responses seen at the Week 16 primary endpoint were sustained to the Week 52 exploratory endpoint. Efficacy assessments, except those at Week 16, were also exploratory endpoints.[1]

Cosentyx is the first IL-17A antagonist and the first biologic other than the current biologic standard of care – anti-TNFs – to demonstrate efficacy in Phase III AS studies.

"I've seen in my patients how painful and debilitating ankylosing spondylitis can be," said Dr. Atul Deodhar, professor of medicine and medical director of Rheumatology Clinics at Oregon Health & Science University, and an investigator in the secukinumab clinical trial program. "These data demonstrate the potential of secukinumab as a new treatment option for ankylosing spondylitis and adds to our growing understanding of the key role IL-17 plays in the pathophysiology of the disease."

Cosentyx was well tolerated in both studies, with a safety profile consistent to that observed in a large psoriasis clinical trial program.[1,3] The most common adverse events (AEs) seen through Week 16 in both studies were nasopharyngitis (upper respiratory tract infection), dyslipidemia (abnormal cholesterol/triglyceride levels), and headache. In MEASURE 1, 68% of Cosentyx patients experienced an AE through Week 16 compared to 56% of placebo patients. Serious adverse event (SAE) rates were 2% for Cosentyx patients and 4% for placebo. In MEASURE 2, 61% of secukinumab patients experienced an AE through Week 16 compared to 64% of placebo patients. SAE rates were 6% for Cosentyx patients and 4% for placebo.[1]

About the MEASURE 1 and MEASURE 2 studies
MEASURE 1 and MEASURE 2 are ongoing, multi-center, randomized, placebo-controlled Phase III studies to evaluate the efficacy and safety of Cosentyx in radiographic-confirmed AS compared to placebo. Both MEASURE 1 and MEASURE 2 evaluated Cosentyx 75 mg and 150 mg vs placebo. In the MEASURE 1 study, patients received an intravenous loading dose

of 10 mg/kg every two weeks for the first four weeks of treatment, followed by monthly subcutaneous doses that aimed to provide high exposure for induction of response. MEASURE 2 evaluated subcutaneous loading regimens.[1]

Secondary endpoints assessed signs and symptoms, physical function and quality of life measures at Week 16 for both studies including: ASAS40 response, change from baseline in high-sensitivity C-reactive protein (hsCRP), ASAS5/6 improvement; changes from baseline in total BASDAI score, Medical Outcomes Study Short Form-36 Health Survey physical component summary score (SF-36 PCS), Ankylosing Spondylitis Quality of Life score (ASQoL) and ASAS partial remission.[1]

- MEASURE 1: primary and all secondary endpoints were met with both Cosentyx groups.[1]
- MEASURE 2: primary and all secondary endpoints except ASAS partial remission were met with Cosentyx 150 mg subcutaneous.[1]
    - Cosentyx 75 mg did not achieve statistical significance vs placebo for primary and any of the secondary endpoints.[1]

Efficacy assessments, except those at Week 16, were exploratory endpoints.[1]

About ankylosing spondylitis (AS)
Ankylosing spondylitis (AS) is a common type of spondyloarthritis (SpA), a spectrum of long-term diseases of joints (inflammatory disease).[4] AS is a painful and often progressively debilitating disease, caused by spine inflammation that can result in irreversible damage.[5] 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.[6] People in their teens and twenties, particularly males, are affected most often. Family members of those with AS are at higher risk.[5,7] Approximately 20-40% of patients do not respond well to standard of care biologic medicines, and there are few therapeutic options available to those people.[8]

About Cosentyx and interleukin-17A (IL-17A)
Cosentyx is not indicated for AS in the US.

Cosentyx (secukinumab), an investigational treatment in AS, is a human monoclonal antibody (mAb) that selectively binds to IL-17A and inhibits its interaction with the IL-17 receptor.[9] Cosentyx is the first IL-17A antagonist with positive results in AS Phase III trials. Research shows that IL-17A plays an important role in driving the body's immune response in certain inflammatory arthritic diseases, including AS.[10]

In January 2015, Cosentyx became the first and only IL-17A antagonist approved in the US by the Food and Drug Administration (FDA) as a treatment for moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy (a drug that is absorbed into the bloodstream and distributed to all parts of the body) or phototherapy (light therapy).

INDICATION
COSENTYX® (secukinumab) is indicated for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

COSENTYX is contraindicated in patients with a previous serious hypersensitivity reaction to secukinumab or to any of the excipients.

WARNINGS AND PRECAUTIONS

Infections
COSENTYX may increase the risk of infections. In clinical trials, a higher rate of infections was observed in subjects treated with COSENTYX compared to placebo-treated subjects. In placebo-controlled clinical trials, higher rates of common infections such as nasopharyngitis (11.4% versus 8.6%), upper respiratory tract infection (2.5% versus 0.7%), and mucocutaneous infections with candida (1.2% versus 0.3%) were observed with COSENTYX compared with placebo. The incidence of some types of infections appeared to be dose-dependent in clinical studies.

Exercise caution when considering the use of COSENTYX in patients with a chronic infection or a history of recurrent infection.

Instruct patients to seek medical advice if signs or symptoms suggestive of an infection occur. If a patient develops a serious infection, the patient should be closely monitored and COSENTYX should be discontinued until the infection resolves.

Pre-treatment Evaluation for Tuberculosis
Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with COSENTYX. Do not administer COSENTYX to patients with active TB infection. Initiate treatment of latent TB prior to administering COSENTYX. Consider anti-TB therapy prior to initiation of COSENTYX in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Patients receiving COSENTYX should be monitored closely for signs and symptoms of active TB during and after treatment.

Exacerbations of Crohn's Disease
Exercise caution when prescribing COSENTYX to patients with active Crohn's disease, as exacerbations of Crohn's disease, in some cases serious, were observed in patients treated with COSENTYX during clinical trials. Patients who are treated with COSENTYX and have active Crohn's disease should be monitored closely.

Hypersensitivity Reactions
Anaphylaxis and cases of urticaria occurred in patients treated with COSENTYX in the clinical trials. If an anaphylactic or other serious allergic reaction occurs, administration of COSENTYX should be discontinued immediately and appropriate therapy initiated.

The removable cap of the COSENTYX Sensoready® pen and the COSENTYX prefilled syringe contains natural rubber latex which may cause an allergic reaction in latex-sensitive individuals. The safe use of the COSENTYX Sensoready pen or prefilled syringe in latex-sensitive individuals has not been studied.

Vaccinations
Prior to initiating therapy with COSENTYX, consider completion of all age appropriate immunizations according to current immunization guidelines. Patients treated with COSENTYX should not receive live vaccines.

Non-live vaccinations received during a course of COSENTYX may not elicit an immune response sufficient to prevent disease.

MOST COMMON ADVERSE REACTIONS

Most common adverse reactions (>1%) are nasopharyngitis, diarrhea, and upper respiratory tract infection.

Please see accompanying full Prescribing Information, including Medication Guide.

Disclaimer
The foregoing release contains forward-looking statements that can be identified by words such as "exploratory," "potential," "growing," "ongoing," "investigational," or similar terms, or by express or implied discussions regarding potential new indications or labeling for Cosentyx (secukinumab), or regarding potential future revenues from Cosentyx. 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 Cosentyx 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 Cosentyx will be commercially successful in the future. In particular, management's expectations regarding Cosentyx could be affected by, among other things, the uncertainties inherent in research and development, including unexpected clinical trial results and additional analysis of existing clinical data; unexpected regulatory actions or delays or government regulation generally; 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
Novartis Pharmaceuticals Corporation researches, develops, manufactures and markets innovative medicines aimed at improving patients' lives. We offer a broad range of medicines for cancer, cardiovascular disease, endocrine disease, inflammatory disease, infectious disease, neurological disease, organ transplantation, psychiatric disease, respiratory disease and skin conditions. The company's mission is to improve people's lives by pioneering novel healthcare solutions.

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 2014, the Group achieved net sales of USD 58.0 billion, while R&D throughout the Group amounted to approximately USD 9.9 billion (USD 9.6 billion excluding impairment and amortization charges). Novartis Group companies employ approximately 120,000 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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