Novartis announces NEJM publication of secukinumab Phase III data confirming significant efficacy in patients with psoriatic arthritis

Sep 30, 2015

- -- In the FUTURE 1 study, secukinumab met the primary endpoint showing statistically significant efficacy versus placebo in improving signs and symptoms of active psoriatic arthritis (PsA)
- -- All pre-specified secondary endpoints were also met, including improvement of skin and joint disease and reduction in progression of joint structural damage
- -- Secukinumab is the first IL-17A antagonist to report positive results in a Phase III PsA trial
- -- PsA is part of a spectrum of long-term diseases impacting joints, known as spondyloarthritis (SpA); new options needed as approximately 45% of patients are dissatisfied with therapies

EAST HANOVER, N.J., Sept. 30, 2015 /PRNewswire/ -- Novartis announced today that results from the pivotal Phase III FUTURE 1 study for secukinumab in psoriatic arthritis (PsA) were published online in The New England Journal of Medicine (NEJM). Secukinumab is the first interleukin-17A (IL-17A) antagonist to demonstrate efficacy in a Phase III study in patients with active PsA, a painful, debilitating condition causing inflammation of joints and skin. PsA is part of a family of long-term diseases impacting joints, known as spondyloarthritis (SpA). There is a high unmet need for new treatment options for patients with PsA and approximately 45% of people are dissatisfied with their treatments.

In this study, secukinumab met the primary endpoint based on a significantly higher percentage of secukinumab patients who achieved at least a 20% reduction in the American College of Rheumatology response criteria (ACR 20) at Week 24 versus placebo. ACR is a standard tool used to assess improvement of PsA signs and symptoms such as tender and swollen joints, pain and disability. In addition, secukinumab met all pre-specified secondary endpoints, including improvements in skin and joint diseases and reduction of joint structural damage progression.

Results showed half of patients (50.0% and 50.5%) in both secukinumab-treated dose groups (150 mg and 75 mg; $p<0.001$) achieved ACR 20 response compared with only 17.3% of placebo patients. Exploratory analyses showed more secukinumab-treated patients in the 150 mg and 75 mg dose groups experienced ACR 20 responses by Week 1 versus placebo ($p<0.001$). In an additional exploratory analysis, a majority of secukinumab-treated patients achieving ACR 20 responses at Week 24 also maintained the response at Week 52 with continued treatment.

"Secukinumab is the first IL-17A antagonist with positive results for the treatment of PsA, further validating the importance of the role IL-17A plays in spondyloarthritis," said Vasant Narasimhan, Global Head of Development, Novartis Pharmaceuticals. "Novartis looks forward to pursuing this important therapy to address the unmet need for patients living with PsA."

Additional, pre-specified subgroup analyses evaluated clinical benefits in patients who had not been previously treated with anti-tumor-necrosis-factor (anti-TNF) therapies (anti-TNF naïve) and also in patients who had an inadequate or no response to anti-TNFs (29.4% of study participants).

Secukinumab was well tolerated in the study, with a safety profile generally consistent with that observed in the psoriasis clinical trial program. The most common adverse events (AEs) for either secukinumab dose were the common cold (nasopharyngitis, 8.2%), headache (5.4%) and upper respiratory tract infections (5.4%). In FUTURE 1, 64.9% (150 mg), 60.4% (75 mg), and 58.4% (placebo) of patients reported an AE. Serious adverse event (SAE) rates were 4.5%, 2.5%, and 5.0%, respectively.

"The pain and discomfort people living with PsA can experience on a daily basis can be truly debilitating," said Philip Mease, MD, clinical professor at the University of Washington School of Medicine in Seattle, director of the Rheumatology Clinical Research Division of Swedish Medical Center, and an investigator in the secukinumab clinical trial program. "These data suggest secukinumab may reduce signs and symptoms of this disease, including inflammation of joints, ligament and tendon insertion sites, and it may reduce the progression of structural damage of the joints. This is important as there remains a need for new and effective treatment options for PsA as not all patients respond to available therapies."

About the FUTURE 1 study
FUTURE 1 is the first multi-center, randomized, placebo-controlled Phase III study to evaluate the efficacy and safety of secukinumab in PsA. The study enrolled 606 patients with active PsA, including patients who had been previously treated with DMARDs (disease-modifying anti-rheumatic drugs) and patients who had an inadequate response or did not tolerate anti-TNFs, and assessed secukinumab with intravenous loading (10 mg/kg) and subcutaneous (75 mg and 150 mg) maintenance dosing. In the study, patients received an intravenous loading dose every two weeks for the first four weeks of treatment followed by monthly subcutaneous doses of 75 mg or 150 mg compared to placebo. The intravenous loading period was designed to provide high systemic exposure for induction of response, in keeping with the initial proof of concept study in PsA with secukinumab.

The study met its primary endpoint, the American College of Rheumatology response criteria (ACR 20), at Week 24:

- 50.5% and 50.0% for secukinumab 75 mg and 150 mg treatment arms, versus 17.3% for placebo; $p<0.001$

Pre-specified secondary endpoints at Week 24 in FUTURE 1 were:

- 75% and 90% improvement in Psoriasis Area-and-Severity Index score (PASI 75 and PASI 90) among subjects with ≥3% of body surface area affected by psoriasis at baseline
- Change from baseline in 28-joint Disease Activity Score using C-reactive protein (DAS28-CRP)
- Quality of life assessed using the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) version 2 physical component summary score
- Physical function assessed using the Health Assessment Questionnaire Disability Index (HAQ-DI)
- ACR 50 response
- Radiographic progression assessed using the van der Heijde modified total Sharp score (mTSS)
- Presence of dactylitis (assessed by dactylitic digit count) and enthesitis (assessed by a four-point enthesitis index) amongst subjects with these characteristics at baseline
- Overall safety and tolerability of each secukinumab regimen compared with placebo

About psoriatic arthritis (PsA)
Closely associated with psoriasis, psoriatic arthritis (PsA) is part of a spectrum of long-term diseases impacting joints, known as spondyloarthritis (SpA). Approximately 30% of patients with psoriasis have psoriatic arthritis. It is a debilitating, long-lasting inflammatory disease linked with significant disability, poor quality of life and reduced life expectancy. PsA is associated with joint pain and stiffness, skin and nail psoriasis, swollen

toes and fingers, persistent painful tendonitis, and irreversible joint damage. Between 0.3% and 1% of the general population may be affected by PsA and as many as one in four people with psoriasis may have undiagnosed PsA.

About secukinumab and interleukin-17A (IL-17A)
Secukinumab is not indicated for PsA.

Secukinumab is a human monoclonal antibody (mAb) that selectively binds to IL-17A and inhibits its interaction with the IL-17 receptor. Secukinumab is the first IL-17A antagonist to report positive results in a PsA Phase III trial. Research shows that IL-17A plays an important role in driving the body's immune response in certain inflammatory arthritic diseases, including PsA. In addition to PsA, secukinumab is also in clinical trials for the treatment of ankylosing spondylitis (AS).

In January 2015, Cosentyx® (secukinumab) became the first and only IL-17A antagonist approved in the US by the 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 "looks forward," "suggest," "may," 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 manufacturing 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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