Novartis announces NEJM publication of two pivotal Phase III secukinumab studies demonstrating statistically significant skin clearance in psoriasis patients

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- - Results of two Phase III psoriasis studies show secukinumab, the first psoriasis IL-17A inhibitor filed with regulatory bodies, met all co-primary and key secondary endpoints[1]
- - A statistically significant percentage of secukinumab-treated patients achieved 75% and 90% skin clearance at Week 12 as measured by PASI 75 and PASI 90[1]
- - A majority of secukinumab-treated patients achieving PASI 75 responses at Week 12 also maintained the response at Week 52 with continued treatment[1]

EAST HANOVER, N.J., July 9, 2014 /PRNewswire/ -- Novartis today announced that The New England Journal of Medicine (NEJM) published the results from two pivotal Phase III studies evaluating the interleukin-17A (IL-17A) inhibitor secukinumab (AIN457). Secukinumab met all primary and key secondary endpoints in the ERASURE and FIXTURE studies, including Psoriasis Area and Severity Index (PASI) 75 and 90 and Investigator's Global Assessment modified 2011 (IGA mod 2011) 0/1 responses.[1] The results of the studies are the first Phase III data for an IL-17A inhibitor to be published in a major scientific journal and were part of the data submitted to the FDA, with action expected early next year.

"These data add to our growing understanding of psoriasis and the key role the IL-17 pathway plays in the pathophysiology of the disease," said Dr. Mark G. Lebwohl, Chair of the Department of Dermatology at the Icahn School of Medicine at Mount Sinai, President-elect of the American Academy of Dermatology and an investigator in the secukinumab clinical trial program. "New and effective treatment options for moderate-to-severe plaque psoriasis are necessary as not every patient responds to existing therapies."

Psoriasis is a chronic autoimmune disease characterized by thick and extensive skin lesions, called plaques, known to cause itching, scaling and pain.[2] The disease affects 7.5 million Americans and can significantly impair physical and psychological quality of life.[3],[4]

PASI measures the redness, scaling and thickness of psoriatic plaques, and the extent of involvement in each region of the body. Treatment efficacy is assessed by the reduction of the score from baseline (ie, a 75% reduction is known as PASI 75 and a 90% reduction is known as PASI 90). PASI 90 is a higher standard of skin clearance compared to PASI 75.

ERASURE Study Design & Results
ERASURE (Efficacy of Response And Safety of two fixed secUkinumab REgimens in psoriasis) was a randomized, double-blind, placebo-controlled, multicenter, parallel-group Phase III study involving 738 patients with moderate-to-severe plaque psoriasis. The co-primary endpoints were assessed at Week 12 and compared secukinumab efficacy versus placebo based on PASI 75 and IGA mod 2011 0/1 responses.[1]

The co-primary and all key secondary endpoints of the study met statistical significance. A higher proportion of

patients treated with secukinumab 300 mg and 150 mg achieved a PASI 75 response at Week 12 compared to placebo patients: 81.6% (300 mg) and 71.6% (150 mg) versus 4.5% for placebo. A higher proportion of patients treated with secukinumab achieved an IGA mod 2011 0/1 response at Week 12 compared to placebo: 65.3% (300 mg) and 51.2% (150 mg), versus 2.4% for placebo.[1]

For the key secondary endpoints at Week 12, 59.2% (300 mg) and 39.1% (150 mg) of secukinumab patients achieved a PASI 90 response compared to 1.2% of placebo patients. The percentage of patients who achieved a PASI 75 response at Week 12 and maintained the response at Week 52 with continued treatment was 80.5% (300 mg) and 72.4% (150 mg). The percentage of patients who achieved an IGA mod 2011 0/1 response at Week 12 and maintained the response at Week 52 with continued treatment was 74.4% (300 mg) and 59.2% (150 mg). Other secondary endpoints included superiority versus placebo in subject-reported, psoriasis-related itching, pain, and scaling scores on the Psoriasis Symptom Diary© at Week 12.[1]

FIXTURE Study Design & Results
FIXTURE (the Full year Investigative eXamination of secukinumab vs. eTanercept Using 2 dosing Regimens to determine Efficacy in psoriasis) was a randomized, double-blind, placebo and active controlled, multicenter, parallel-group Phase III study involving 1306 patients with moderate-to-severe plaque psoriasis.[1] In this single study with etanercept as active control, the etanercept used was EU-approved and not US-licensed. The co-primary endpoints were assessed at Week 12 and compared secukinumab efficacy versus placebo based on PASI 75 and IGA mod 2011 0/1 responses.[1]

The co-primary and all key secondary endpoints of the study met statistical significance. A higher proportion of patients treated with secukinumab 300 mg and 150 mg achieved a PASI 75 response at Week 12 compared to placebo and etanercept: 77.1% (300 mg) and 67.0% (150 mg), versus 4.9% for placebo and 44.0% for etanercept. A higher proportion of patients treated with secukinumab also achieved an IGA mod 2011 0/1 response at Week 12 compared to placebo and etanercept: 62.5% (300 mg) and 51.1% (150 mg), versus 2.8% for placebo and 27.2% for etanercept.[1]

For the key secondary endpoints, 54.2% (300 mg) and 41.9% (150 mg) of secukinumab-treated patients achieved a PASI 90 response at Week 12 compared to 1.5% of placebo and 20.7% of etanercept patients. A higher proportion of secukinumab-treated patients who achieved a PASI 75 response at Week 12 maintained the response at Week 52 with continued treatment compared to etanercept: 84.3% (300 mg) and 82.2% (150 mg) versus 72.5% for etanercept. The percentage of secukinumab patients who achieved an IGA mod 2011 0/1 response at Week 12 and maintained the response at Week 52 with continued treatment was 79.7% (300 mg) and 67.7% (150 mg) compared to 56.8% of etanercept patients. Other secondary endpoints included superiority versus placebo in subject-reported, psoriasis-related itching, pain, and scaling scores on the Psoriasis Symptom Diary© at Week 12.[1]

"Plaque psoriasis can be a painful and debilitating chronic disease and we are pleased that secukinumab could be an important treatment for patients with moderate-to-severe symptoms who need new options," said Christi Shaw, President, Novartis Pharmaceuticals Corporation and President, Novartis Corporation. "The publication of the Phase III data in NEJM validates the significance of the studies and draws attention to the major unmet need in this disease. Novartis will continue working with investigators and the FDA to bring secukinumab to patients as soon as possible."

In ERASURE, the most common adverse events (AEs) in any treatment group including placebo (n=738) were nasopharyngitis, headache, and upper respiratory tract infection. Eighteen patients in the secukinumab 300 mg arm, 12 patients in the secukinumab 150 mg arm, and five patients in the placebo group discontinued the study due to AEs. Serious AEs during the entire treatment period were reported at rates (in events per 100 subject-years) of 6.3 (300 mg), 6.4 (150 mg), and 7.4 (placebo).[1]

In FIXTURE, the most common AEs in any treatment group including etanercept and placebo (n=1,306) were nasopharyngitis, headache, and diarrhea. Fourteen patients in the secukinumab 300 mg arm, 10 patients in the secukinumab 150 mg arm, 12 patients in the etanercept arm and three patients in the placebo arm discontinued due to AEs. Serious AEs during the entire treatment period were reported at rates (in events per 100 subject-years) of 6.8 (300 mg), 6.0 (150 mg), 7.0 (etanercept), and 8.3 (placebo) with no clinically apparent differences in the type of SAEs among treatment groups. There were no deaths reported although there was one death unrelated to psoriasis during the FIXTURE screening period.[1]

About secukinumab (AIN457) and interleukin-17A (IL-17A)
Secukinumab (AIN457), an investigational agent, is a fully human monoclonal antibody (mAb) that selectively targets interleukin IL-17A.[5] Secukinumab has been shown to selectively bind to and neutralize IL-17A, inhibiting its pro-inflammatory effects.[6],[7]

IL-17A is a key cytokine (messenger protein) involved in the development of plaque psoriasis, and is found in high concentrations in psoriasis skin plaques.[8] Research shows that IL-17A plays an important role in driving the body's immune response in disorders such as moderate-to-severe plaque psoriasis and may represent a new target for investigational therapies.[9],[10]

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[1] Langley RG, Elewski BE, Lebwohl M, et al. Secukinumab in Plaque Psoriasis: Results of Two Phase Three Trials.

N Engl J Med . 2014; [published online ahead of print 9 July 2014]

[2] Nestle FO, Kaplan DH, Barker J. Psoriasis. New Engl J Med. 2009; 361: 496-509.

[3] National Psoriasis Foundation. Statistics. Available here: http://www.psoriasis.org/research/science-of-psoriasis/statistics. Accessed April 1, 2014.

[4] de Korte J, Sprangers MA, Mombers FM, Bos JD. Quality of life in patients with psoriasis: a systematic literature review. J Investig Dermatol Symp Proc. 2004;9:140-7.

[5] Patel D. Effect of IL-17A blockade with secukinumab in autoimmune diseases. Ann Rheum Dis. 2013; 72:116-123.

[6] Papp KA, Langley RG, Sigurgeirsson B, et al. Efficacy and safety of secukinumab in the treatment of moderate- to-severe plaque psoriasis: a randomized, double-blind, placebo-controlled phase II dose-ranging study. Brit J Dermatol 2013; 168, pp412-421.

[7] Rich PA, Sigurgeirsson B, Thaci D, et al. Secukinumab induction and maintenance therapy in moderate-to-severe plaque psoriasis: a randomized, double-blind, placebo-controlled, phase II regimen-finding study. Brit J Dermatol. 2013;168: 402-411.

[8] Johansen C, Usher PA, Kjellerup RB, et al. Characterization of the interleukin-17 isoforms and receptors in lesional psoriatic skin Brit J Dermatol. 2009; 160:319-24.

[9] Gaffen SL. Structure and signaling in the IL-17 receptor family. Nat Rev Immunol. 2009; 9(8):556-67.

[10] Krueger J, Fretzin S, Suárez-Fariñas M, et al. IL-17A is essential for cell activation and inflammatory gene circuits in subjects with psoriasis. J Allergy Clin Immunol. 2012; 130(1):145-154.

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