



Lilly's Anti-IL-17 Monoclonal Antibody, Ixekizumab, Met Primary Endpoint in Phase II Study in Patients With Chronic Plaque Psoriasis

- Results published in New England Journal of Medicine showed significantly more patients achieved improvements in skin disease severity scores compared with placebo -

INDIANAPOLIS, March 28, 2012 /PRNewswire/ -- New Phase II data, published today in the *New England Journal of Medicine*, showed that Eli Lilly and Company's (NYSE: LLY) ixekizumab (pronounced ix' e kiz' ue mab, previously known as LY2439821), an anti-IL-17 monoclonal antibody, met its primary endpoint in patients with moderate-to-severe plaque psoriasis, with significantly more patients achieving at least a 75 percent improvement in Psoriasis Area and Severity Index (PASI) scores from baseline (PASI 75) compared with placebo at week 12.

PASI score represents a combined assessment of overall skin lesions ranging from 0 for no psoriasis to 72 for the worst possible psoriasis in a patient and is a standard measure of skin disease severity in clinical trials in psoriasis. A PASI 75 response in a patient represents a 75 percent reduction of PASI scores from baseline.

In the 142-subject study, significantly more patients achieved a PASI 75 response in the 150 mg (82 percent), 75 mg (83 percent) and 25 mg (77 percent) ixekizumab groups compared with placebo (8 percent, $p < 0.001$) at week 12. The 10 mg dose (29 percent) did not separate from placebo at week 12.

Secondary endpoints included an evaluation of the percentage of patients achieving at least 90 percent and 100 percent improvement in PASI (PASI 90 or PASI 100) at week 12. In patients treated with ixekizumab, the percentages of patients achieving a PASI 90 response were 71 percent (150 mg), 59 percent (75 mg) and 50 percent (25 mg), which were significantly higher than with placebo (0 percent). PASI 100 responses were significantly better at the 150 mg dose (39 percent) and 75 mg dose (38 percent) when compared with placebo (0 percent). PASI 100 responses at the 25 mg (17 percent) and 10 mg doses (0 percent) were not significantly greater than placebo, nor was the PASI 90 response at the 10 mg dose (18 percent).

PASI 75 response was significantly better than placebo as early as week 2 at the highest dose, and significant differences from placebo in PASI scores were seen as early as week 1 at the two highest doses and by week 4 for the remaining two doses. Differences from placebo were sustained to week 20 in both PASI 75 responses and PASI scores.

Skin disease severity also was evaluated by static Physician Global Assessments (sPGA), with patients having a score of 3-5 (moderate to severe disease) at baseline. Significantly more patients treated with ixekizumab achieved an sPGA score of 0 (clear of disease) or 1 (minimal disease), when compared with placebo at week 12. The percentage of patients achieving an sPGA 0 or 1 score were 71 percent (150 mg), 72 percent (75 mg), 70 percent (25 mg) and 25 percent (10 mg) compared with 8 percent (placebo), with the highest three doses being significantly higher than placebo. The percentage of patients achieving an sPGA score of 0 at week 12 were 46 percent (150 mg), 38 percent (75 mg), 20 percent (25 mg), 7 percent (10 mg) and 0 percent (placebo), again with the highest three ixekizumab doses being significantly higher than placebo.

Approximately 40 percent of patients in the two highest dose groups had complete clearance of psoriasis plaques on the skin, as reflected by a reduction in the PASI score by 100 percent or an sPGA score of 0 at 12 weeks.

In addition, significant reductions in mean Nail Psoriasis Severity Index (NAPSI) and Psoriasis Scalp Severity Index (PSSI), which evaluate disease in the difficult-to-treat areas of nails and scalp, respectively, were seen at the two highest ixekizumab doses compared with placebo at week 12 (NAPSI: 150 mg [-49.3 percent], 75 mg [-57.1 percent], placebo [+6.8 percent]; PSSI: 150 mg [-84.8 percent], 75 mg [-94.8 percent], placebo [-30.5 percent]).

The frequency of adverse events in both the combined ixekizumab groups and in the placebo group was 63 percent, with the most common adverse events observed being nasopharyngitis (inflammation of the nasal passages and of the upper part of the pharynx), upper respiratory infection, injection site reactions and headache. There were no serious adverse events reported. Infections occurred in 33 percent (38 patients) of subjects receiving ixekizumab and 26 percent (seven patients) receiving placebo. No dose-related trends in infections or other adverse events were observed. Four patients (one in the placebo group, two in the 10 mg group and one in 25 mg group) discontinued the study due to adverse events.

"These data suggest ixekizumab may be an effective treatment for patients with chronic moderate-to-severe plaque psoriasis and could represent a new treatment approach for patients with this condition," said Craig Leonardi, M.D., clinical professor of

dermatology at the Saint Louis University School of Medicine, and lead author of the manuscript. "Further studies are needed, but we are encouraged by the results showing improvements in skin clearance early in treatment."

Psoriasis is the most prevalent chronic, autoimmune disease of the skin in the United States, affecting about 7.5 million people. It occurs when the immune system sends out faulty signals that speed up the growth cycle of skin cells. Approximately 17 percent of psoriasis patients have moderate-to-severe plaque psoriasis.[1]

"While there are a number of commonly used treatments for autoimmune diseases, new and alternative treatment options are needed for those impacted by these potentially debilitating conditions, including psoriasis," said Eiry Roberts, M.D., vice president of autoimmune product development at Lilly. "We are committed to developing new autoimmune therapies such as ixekizumab, which was discovered in our own research labs and is now being studied in Phase III for psoriasis."

About the Study

A total of 142 patients with chronic moderate-to-severe plaque psoriasis participated in the randomized, double-blind, placebo-controlled, parallel-group, dose-ranging study. Patients were randomized to receive subcutaneous injections of placebo or 10 mg, 25 mg, 75 mg or 150 mg of ixekizumab at weeks 0, 2, 4, 8, 12 and 16. Data were collected at baseline, and weeks 1, 2, 4, 6, 8, 12, 16 and 20.

To view the published manuscript, please visit www.nejm.org.

About Ixekizumab

Ixekizumab is a humanized monoclonal antibody that binds to and neutralizes actions of the pro-inflammatory cytokine, interleukin-17A (IL-17A, also called IL-17), and is administered via subcutaneous injection. Ixekizumab is currently in Phase III testing for psoriasis and is being evaluated as a potential treatment for psoriatic arthritis, rheumatoid arthritis and ankylosing spondylitis.

About Psoriasis

The most common form of psoriasis, plaque psoriasis, appears as raised, red patches covered with a silvery white buildup of dead skin cells. Psoriasis can occur on any part of the body and is associated with other serious health conditions, such as diabetes, and heart disease.[2], [3]

Psoriasis involving scalp, nails, and palms and soles is hard to treat.[4] Despite the availability of biologics and topical treatments, patients are still in need of new and alternative treatment options to treat the disease.

About Eli Lilly and Company

Lilly, a leading innovation-driven corporation, is developing a growing portfolio of pharmaceutical products by applying the latest research from its own worldwide laboratories and from collaborations with eminent scientific organizations. Headquartered in Indianapolis, Ind., Lilly provides answers — through medicines and information — for some of the world's most urgent medical needs. Additional information about Lilly is available at www.lilly.com.

This press release contains certain forward-looking statements about ixekizumab as a potential treatment for patients with chronic plaque psoriasis and reflects Lilly's current beliefs. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization. There is no guarantee that future study results and patient experience will be consistent with study findings to date or that the product will be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's filings with the United States Securities and Exchange Commission. Lilly undertakes no duty to update forward-looking statements.

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[1] National Psoriasis Foundation, "About Psoriasis," <http://psoriasis.org/about-psoriasis>. Accessed March 23, 2012.

[2] Rapp SR, Feldman SR, Exum ML, Fleischer AB, Reboussin DM. Psoriasis causes as much disability as other major medical diseases. *J Am Acad Dermatol* 1999;41:401-7.

[3] Kurd SK, et al. The Risk of Depression, Anxiety, and Suicidality in Patients With Psoriasis. *Arch Dermatol.* 2010;146(8):891-895.

[4] National Psoriasis Foundation, "Psoriasis on Specific Locations," <http://www.psoriasis.org/about-psoriasis/specific-locations>. Accessed March 23, 2012.

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