Lilly Announces Positive Top-Line Results for COAST-X, a 52-Week Placebo-Controlled Study of Taltz® (ixekizumab) in Patients with Non-Radiographic Axial Spondyloarthritis

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INDIANAPOLIS, April 22, 2019 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) announced today that Taltz® (ixekizumab) met the primary and all major secondary endpoints in COAST-X, a Phase 3 study evaluating the safety and efficacy of Taltz for the treatment of non-radiographic axial spondyloarthritis (nr-axSpA) in patients who are biologic disease-modifying anti-rheumatic drug (bDMARD)-naïve. These results provide clinical evidence to support a potential role for Taltz in the treatment of nr-axSpA patients.

Taltz met the primary endpoint at both week 16 and week 52, demonstrating a statistically significant improvement in the signs and symptoms of nr-axSpA, as measured by the proportion of patients who achieved Assessment of Spondyloarthritis International Society 40 (ASAS40) response compared to placebo.

Taltz also met the major secondary endpoints at week 16 and week 52, including significant improvement in Ankylosing Spondylitis Disease Activity Score (ASDAS), significant improvement in Bath Ankylosing Spondylitis Disease Activity (BASDAI), proportion of patients achieving low disease activity (ASDAS <2.1), significant improvement in sacroiliac joint inflammation (SIJ) as assessed by MRI (week 16) and significant improvement in 36-Item Short Form Health Survey (SF-36) Physical Component Summary (PCS) Score.

In COAST-X, the safety profile of Taltz was consistent with previously reported Phase 3 studies of Taltz. No new safety signals were detected.

"Non-radiographic axSpA is a challenging diagnosis that is not only missed in clinics, but also has limited treatment options for physicians to offer patients," said Atul Deodhar, M.D., professor of medicine, Oregon Health & Science University and clinical investigator for the COAST program. "The COAST-X results offer compelling evidence that Taltz could provide a much-needed new alternative if approved for this patient population."

Axial spondyloarthritis (axSpA) is a chronic inflammatory disease affecting predominantly the sacroiliac joints and the axial skeleton and is estimated to affect 4.5 million adults worldwide.[1,2,3] AxSpA is recognized as a single disease entity, with a patient subset defined by the presence of radiographically defined structural damage of the sacroiliac joints (radiographic axSpA or ankylosing spondylitis [AS]) and a patient subset without clear structural damage radiographically (nr-axSpA).[4] These two patient subsets share a similar burden of disease and similar clinical features, such as spinal inflammation and chronic inflammatory back pain.[5,6] The COAST-X study is part of a clinical development program that aims to evaluate the efficacy and safety of Taltz across various population subsets of patients with axSpA. Results from COAST-V and COAST-W, which evaluated Taltz in AS, were reported in 2018.

"We're encouraged by the results of the COAST-X trial, which support our belief that Taltz could become the first IL-17A antagonist to be approved in the U.S. for people with non-radiographic axSpA," said Christi Shaw, president, Lilly Bio-Medicines. "The COAST-X data add to the growing body of evidence from our COAST program, which demonstrates that Taltz may work across the axSpA disease spectrum."

Lilly plans to submit detailed data from COAST-X for disclosure at scientific meetings and in peer-reviewed journals later this year. Based on these positive data, Lilly plans to submit to regulatory authorities in 2019 for approval for nr-axSpA.

Lilly's application for radiographic axSpA is currently under review with the U.S. Food and Drug Administration (FDA) and regulatory action is expected later this year.

INDICATIONS AND USAGE FOR TALTZ (ixekizumab) injection
Taltz is approved for the treatment of adults with active psoriatic arthritis. Taltz is also approved to treat adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

IMPORTANT SAFETY INFORMATION FOR TALTZ

CONTRAINDICATIONS
Taltz is contraindicated in patients with a previous serious hypersensitivity reaction, such as anaphylaxis, to ixekizumab or to any of the excipients.

WARNINGS AND PRECAUTIONS

Infections
Taltz may increase the risk of infection. In clinical trials of patients with plaque psoriasis, the Taltz group had a higher rate of infections than the placebo group (27% vs 23%). A similar increase in risk of infection was seen in placebo-controlled trials of patients with psoriatic arthritis. Serious infections have occurred. Instruct patients to seek medical advice if signs or symptoms of clinically important chronic or acute infection occur. If a serious infection develops, discontinue Taltz until the infection resolves.

Pre-Treatment Evaluation for Tuberculosis
Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with Taltz. Do not administer to patients with active TB infection. Initiate treatment of latent TB prior to administering Taltz. Closely monitor patients receiving Taltz for signs and symptoms of active TB during and after

treatment.

Hypersensitivity
Serious hypersensitivity reactions, including angioedema and urticaria (each ≤0.1%), occurred in the Taltz group in clinical trials. Anaphylaxis, including cases leading to hospitalization, has been reported in post-marketing use with Taltz. If a serious hypersensitivity reaction occurs, discontinue Taltz immediately and initiate appropriate therapy.

Inflammatory Bowel Disease
Crohn's disease and ulcerative colitis, including exacerbations, occurred at a greater frequency in the Taltz group (Crohn's disease 0.1%, ulcerative colitis 0.2%) than in the placebo group (0%) during clinical trials in patients with plaque psoriasis. During Taltz treatment, monitor patients for onset or exacerbations of inflammatory bowel disease.

Immunizations
Prior to initiating therapy with Taltz, consider completion of all age-appropriate immunizations according to current immunization guidelines. Avoid use of live vaccines in patients treated with Taltz.

ADVERSE REACTIONS
Most common adverse reactions (>1%) associated with Taltz treatment are injection site reactions, upper respiratory tract infections, nausea, and tinea infections. Overall, the safety profile observed in patients with psoriatic arthritis was consistent with the safety profile in patients with plaque psoriasis, with the exception of influenza and conjunctivitis.

Please see accompanying Prescribing Information and Medication Guide. Please see Instructions for Use included with the device.

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About Taltz®
Taltz (ixekizumab) is a monoclonal antibody that selectively binds with interleukin 17A (IL-17A) cytokine and inhibits its interaction with the IL-17 receptor.[7] IL-17A is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Taltz inhibits the release of pro-inflammatory cytokines and chemokines.[7]

About COAST-X
COAST-X is a multicenter, randomized, double-blind, placebo-controlled 52-week study evaluating the efficacy and safety of Taltz (ixekizumab) for the treatment of non-radiographic axial spondyloarthritis (nr-axSpA) in patients who are biologic disease-modifying anti-rheumatic drug (bDMARD)-naïve. Patients were required to have an established diagnosis of nr-axSpA and active disease defined by a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) Numeric Rating Scale (NRS) score ≥4 and total back pain ≥4 at screening and baseline, and were required to have objective signs of inflammation by presence of sacroiliitis on MRI or presence of elevated CRP.

About the Taltz Program in axSpA
The COAST-X study is part of a clinical development program that aims to evaluate the efficacy and safety of ixekizumab across various population subsets of patients with axSpA. The COAST program includes three registration studies each of one year duration: COAST-V in patients with Ankylosing Spondylitis (AS)/radiographic axSpA who are bDMARD-naïve; COAST-W in patients with AS/radiographic axSpA who previously had an inadequate response or were intolerant to TNF inhibitors; and COAST-X in patients with non-radiographic axSpA who are bDMARD-naïve. Patients may enroll into a long-term extension study after completion of any of the registration studies to receive ixekizumab treatment for up to an additional two years (COAST-Y).

About Lilly in Immunology
Lilly is bringing our heritage of championing groundbreaking, novel science to immunology and is driven to change what's possible for people living with autoimmune diseases. There are still significant unmet needs, as well as personal and societal costs, for people living with a variety of autoimmune diseases and our goal is to minimize the burden of disease. Lilly is investing in leading-edge clinical approaches across its immunology portfolio in hopes of transforming the autoimmune disease treatment experience. We've built a deep pipeline and are focused on advancing cutting edge science to find new treatments that offer meaningful improvements to support the people and the communities we serve.

About Eli Lilly and Company
Lilly is a global healthcare leader that unites caring with discovery to create medicines that make life better for people around the world. We were founded more than a century ago by a man committed to creating high-quality medicines that meet real needs, and today we remain true to that mission in all our work. Across the globe, Lilly employees work to discover and bring life-changing medicines to those who need them, improve the understanding and management of disease, and give back to communities through philanthropy and volunteerism. To learn more about Lilly, please visit us at www.lilly.com and www.lilly.com/newsroom/social-channels. P-LLY

This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about Taltz (ixekizumab) as a treatment for moderate-to-severe plaque psoriasis and active psoriatic arthritis and as a potential treatment for non-radiographic axial spondyloarthritis and ankylosing spondylitis, and reflects Lilly's current belief. As with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization. Among other things, there can be no guarantee that future study results will be consistent with the results to date, that Taltz will receive additional regulatory approvals, or be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's most recent Form 10-K and Form 10-Q filings with the United States Securities and Exchange Commission. Except as required by law, Lilly undertake no duty to update forward-looking statements to reflect events after the date of this release.

[1] Spondyloarthritis. Arthritis Foundation. https://www.arthritis.org/about-arthritis/types/spondyloarthritis/. Accessed March 7, 2019.

[2] Strand V, Rao SA, Shillington AC, et al. Prevalence of axial spondyloarthritis in United States rheumatology practices: Assessment of SpondyloArthritis International Society criteria versus rheumatology expert clinical diagnosis. *Arthritis Care Res.* 2013;65(8):1299-306.

[3] Kiltz U, Baraliakos X, Karakostas P, et al. Do patients with non-radiographic axial spondylarthritis differ from patients with ankylosing spondylitis? *Arthritis Care Res.* 2012;64(9):1415-22.

[4] Deodhar A, Reveille JD, van den Bosch F, et al. The concept of axial spondyloarthritis: joint statement of the spondyloarthritis research and treatment network and the Assessment of SpondyloArthritis International Society in response to the US Food and Drug Administration's comments and concerns. *Arthritis Rheumatol*. 2014;66(10):2649-2656.

[5] Baraliakos X, Braun J. Non-radiographic axial spondyloarthritis and ankylosing spondylitis: what are the similarities and differences? *RMD Open.* 2015;1:e000053.

[6] Taurog JD, Chhabra A, Colbert RA. Ankylosing spondylitis and axial spondyloarthritis. *N Engl J Med.* 2016,374(26):2563-74.

[7] Taltz Prescribing Information, 2018.

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