ACR 2019: Lilly Presents Positive New Data from COAST-X, a Phase 3 Study of Taltz® (ixekizumab) in Patients with Non-Radiographic Axial Spondyloarthritis

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Based on these positive results, Lilly has submitted for U.S. regulatory approval for adults with active non-radiographic axial spondyloarthritis

INDIANAPOLIS, Nov. 12, 2019 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) presented detailed results today demonstrating Taltz® (ixekizumab) met the primary and all major secondary endpoints in COAST-X, a 52-week placebo-controlled Phase 3 study evaluating the safety and efficacy of Taltz for the treatment of non-radiographic axial spondyloarthritis (nr-axSpA) in patients with objective signs of inflammation who are biologic disease-modifying anti-rheumatic drug (bDMARD)-naïve. The data are being presented at the American College of Rheumatology (ACR)/Association of Rheumatology Professionals (ARP) Annual Meeting in Atlanta as a plenary presentation.

"In the COAST-X study, Taltz improved the signs and symptoms of non-radiographic axSpA as measured by ASAS40, as well as reduced inflammation on MRI, an important objective measure of disease activity," said Atul Deodhar, M.D., professor of medicine, Oregon Health & Science University and clinical investigator for the COAST program. "If approved for this patient population, Taltz could be an important treatment option to help address chronic, debilitating symptoms for people living with non-radiographic axSpA."

Axial spondyloarthritis (axSpA) is a chronic inflammatory disease affecting predominantly the sacroiliac joints and the spine 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 clearly detectable structural damage radiographically (nr-axSpA).[4] These two patient subsets share a similar burden of disease and similar clinical features, such as inflammation in the axial skeleton, resulting in chronic inflammatory back pain and fatigue, but the biologic treatment options for patients with nr-axSpA are much more limited.[5,6]

"We're pleased to share these positive results from the COAST-X trial, which support our belief that Taltz could be an effective treatment option for patients with non-radiographic axSpA," said Rhonda Pacheco, Pharm.D., global brand development leader for immunology at Lilly. "We look forward to working with regulatory authorities towards our goal of making Taltz the first IL-17A antagonist approved for non-radiographic axSpA."

A total of 303 adult patients with active nr-axSpA were randomized to receive Taltz 80 mg subcutaneously every 4 weeks or every 2 weeks (following 80 mg or 160 mg starting dose at Week 0) or placebo. The proportion of patients achieving the primary endpoint of improvement in the signs and symptoms of nr-axSpA as measured by Assessment of Spondyloarthritis International Society 40 (ASAS40) response was superior for Taltz compared to placebo with statistically significant difference ($P<0.01$):

- At Week 16, 35 percent of patients treated with Taltz every four weeks and 40 percent of patients treated with Taltz every two weeks achieved ASAS40 response, compared to 19 percent of patients treated with placebo.
- At Week 52, 30 percent of patients treated with Taltz every four weeks and 31 percent of patients treated with Taltz every two weeks achieved ASAS40 response, compared to 13 percent of patients treated with placebo.

Taltz also met the major secondary endpoints in the study 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 as assessed by MRI (Week 16) and significant improvement in 36-Item Short Form Health Survey (SF-36) Physical Component Summary (PCS) Score.

The overall safety profile of Taltz was consistent with previously reported results, with no new or unexpected safety findings.

INDICATIONS AND USAGE FOR TALTZ
Taltz is approved for the treatment of adults with adults with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy. Taltz is also approved for the treatment of adults with active psoriatic arthritis and active ankylosing spondylitis.

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 and ankylosing spondylitis. 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
During Taltz treatment, monitor patients for onset or exacerbations of inflammatory bowel disease. Crohn's disease and ulcerative colitis, including exacerbations, occurred at a greater frequency in the Taltz 80 mg Q2W group (Crohn's disease 0.1%, ulcerative colitis 0.2%) than in the placebo group (0%) during clinical trials in patients with plaque psoriasis and in the Taltz Q4W group in ankylosing spondylitis trials (Crohn's disease 1.0% [2 patients], ulcerative colitis 0.5% [1 patient]) than in the placebo group (Crohn's disease 0.5% [1 patient], ulcerative colitis 0%). In the ankylosing spondylitis trials, serious events occurred in 1 patient in the Taltz group and 1 patient in the placebo group.

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 profiles observed in patients with psoriatic arthritis and ankylosing spondylitis were consistent with the safety profile in patients with plaque psoriasis, with the exception of influenza and conjunctivitis in psoriatic arthritis.

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 (COAST-Y) after completion of any of these registration studies to receive ixekizumab treatment for up to an additional two years.

About Lilly in Rheumatology
Lilly in Rheumatology aims to create a brighter future for people with debilitating rheumatologic diseases through innovative discoveries and patient-centered solutions.

About Eli Lilly and Company
Lilly is a global health care 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 lilly.com and lilly.com/newsroom. 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 potential treatment for patients with active non-radiographic axial spondyloarthritis, and reflects Lilly's current belief. However, 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 October 16, 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, 2019.

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