ACR 2018: Lilly Announces Positive Results for Two Phase 3 Studies of Taltz® (ixekizumab) in Ankylosing Spondylitis (Radiographic Axial Spondyloarthritis)

October 22, 2018

- COAST-V is the first successful AS trial to use ASAS40 as the primary endpoint -

- COAST-W is the first AS trial to specifically focus on patients who had failed one or two tumor necrosis factor (TNF) inhibitors or are intolerant to a TNF inhibitor and to generate data on spinal MRI inflammation in this patient population -

INDIANAPOLIS, Oct. 22, 2018/PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) announced today that the company will present positive findings from two Phase 3 studies, COAST-V and COAST-W, in adults with ankylosing spondylitis (AS), also referred to as radiographic axial spondyloarthritis (axSpA), at the American College of Rheumatology (ACR)/Association of Rheumatology Health Professionals (ARHP) Annual Meeting in Chicago on October 23. The analyses are part of a clinical development program that aims to evaluate Taltz® (ixekizumab) across various populations of patients with AS.

"Many people with AS are either untreated or still searching for an effective treatment," said Lotus Mallbris, M.D., Ph.D., vice president of immunology development at Lilly. "By using ASAS40 as the primary endpoint in our clinical development program, we hope to establish a higher treatment bar for AS patients."

In both studies, Taltz demonstrated a statistically significant and clinically meaningful improvement in proportion of patients who achieved Assessment of Spondyloarthritis International Society 40 (ASAS40) over 16 weeks compared to placebo. ASAS40 represents at least a 40-percent improvement in disease signs and symptoms such as pain, inflammation and function. COAST-V is the first successful trial in AS to use ASAS40, a stringent clinical measure indicating a high degree of clinical improvement as the primary endpoint, compared to the standard endpoint of ASAS20. COAST-W is the first AS study to specifically focus on the difficult-to-treat population of patients who had an inadequate response to one or two tumor necrosis factor (TNF) inhibitors (90 percent of enrolled patients) or intolerance to a TNF inhibitor (10 percent).

COAST-V Analysis of Study Results

COAST-V, which included 341 patients, is the first Phase 3 study of Taltz among patients with AS who had never received a biologic disease-modifying anti-rheumatic drug (bDMARD). It also is the first study to include both a placebo control arm and active reference arm (adalimumab). During the study, patients were treated with 80 mg of Taltz subcutaneously either every four weeks or every two weeks (following 80 mg or 160 mg starting dose at Week 0), adalimumab, or placebo.At 16 weeks, 48 percent of patients treated with Taltz every four weeks, 52 percent of patients treated with Taltz every two weeks and 18 percent of patients treated with placebo achieved ASAS40, the primary endpoint of the study.

Taltz also demonstrated a statistically significant improvement on the following secondary endpoints, achieving the following response rates at 16 weeks:

- **ASAS20:** 64 percent of patients treated with Taltz every four weeks, 69 percent of patients treated with Taltz every two weeks and 40 percent of patients treated with placebo achieved ASAS20.
- **BASDAI50:** 42 percent of patients treated with Taltz every four weeks, 43 percent of patients treated with Taltz every two weeks and 17 percent of patients treated with placebo achieved a Bath Ankylosing Spondylitis Disease Activity Index 50 (BASDAI50).
- **MRI Spine SPARCC CFB:** patients treated with Taltz every four weeks experienced a -11.0 change from baseline (CFB) in MRI spine SpA Research Consortium of Canada (SPARCC) score, patients treated with Taltz every two weeks experienced a -9.6 SPARCC CFB and patients treated with placebo experienced a -1.5 SPARCC CFB.

"Taltz demonstrated significant improvements in disease activity, functional disability, and spinal and sacroiliac joint inflammation among patients with AS," said Désirée van der Heijde, M.D., Ph.D., professor of rheumatology at Leiden University Medical Center.

COAST-W Analysis of Study Results

COAST-W is a Phase 3 study of 316 patients with AS who had an inadequate response or were intolerant to one or two tumor necrosis factor (TNF) inhibitors. COAST-W is the first dedicated study to measure the effect of biologic therapy in this patient population including spinal inflammation in patients with AS by using magnetic resonance imaging (MRI). During the study, patients were treated with 80 mg of Taltz subcutaneously either every four weeks or every two weeks (following 80 mg or 160 mg starting dose at Week 0), or placebo. At 16 weeks, 25 percent of patients treated with Taltz every four weeks, 31 percent of patients treated with Taltz every two weeks and 13% of patients treated with placebo achieved ASAS40, the primary endpoint of the study.

In addition, patients treated with Taltz achieved the following response rates at 16 weeks:

- **ASAS20:** 48 percent of patients treated with Taltz every four weeks, 47 percent of patients treated with Taltz every two weeks and 30 percent of patients treated with placebo achieved ASAS20.

- **BASDAI CFB:** patients treated with Taltz every four weeks and patients treated with Taltz every two weeks experienced a statistically significant reduction in disease activity compared to placebo as measured by BASDAI (-2.2±0.2 , -2.1±0.2 and -0.9±0.2 respectively).
- **MRI SPARCC Spine CFB:** patients treated with Taltz every four weeks and patients treated with Taltz every two weeks experienced a statistically significant reduction in spinal MRI inflammation compared to placebo as measured by the CFB in MRI spine SPARCC score (-3.0, -4.0 and 3.3, respectively).

In both COAST-V and COAST-W, the 80 mg Q2W and Q4W dosing regimens demonstrated similar safety profiles. There were no new or unexpected safety findings in the AS population, compared to the psoriasis and psoriatic arthritis populations.
The COAST-V Phase 3 data has been published within *The Lancet* and the COAST-W Phase 3 data has been published within *Arthritis & Rheumatology.*

Based on the positive results from the COAST-V and COAST-W studies, the company plans to submit for U.S. regulatory approval in AS/radiographic axSpA later this year.

INDICATIONS AND USAGE FOR TALTZ
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 the Taltz Program in axSpA
The COAST-V and COAST-W studies are 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 studies, each of one-year duration: COAST-V in patients with AS/active radiographic axSpA who are bDMARD-naïve; COAST-W in patients with AS/active radiographic axSpA who previously had an inadequate response or intolerance 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 studies to receive ixekizumab treatment for up to an additional two years.

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. 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.

About Eli Lilly and Company
Lilly is a global healthcare leader that unites caring with discovery to 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 potential treatment for ankylosing spondylitis (AS), also referred to as radiographic axial spondyloarthritis (axSpA), 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 or 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 undertakes no duty to update forward-looking statements to reflect events after the date of this release.

Refer to:	Jackie Shelton, sheltonj@lilly.com; 317-719-5928 (media)
	Kevin Hern; hern_kevin_r@lilly.com; 317-277-1838 (investors)

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