Pfizer and Lilly Announce Top-Line Results From Long-Term Phase 3 Study of Tanezumab in Patients With Osteoarthritis

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NEW YORK & INDIANAPOLIS--(BUSINESS WIRE)-- Pfizer Inc. (NYSE:PFE) and Eli Lilly and Company (NYSE:LLY) today announced top-line results from a Phase 3 study evaluating tanezumab 2.5 mg and 5 mg. The objective of the study was to compare the long-term joint safety and 16-week efficacy of tanezumab relative to nonsteroidal anti-inflammatory drugs (NSAIDs) in patients with moderate-to-severe osteoarthritis (OA) of the hip or knee. The tanezumab 5 mg treatment arm met two of the three co-primary efficacy endpoints, demonstrating a statistically significant improvement in pain and physical function compared to NSAIDs at the 16-week analysis, while patients' overall assessment of their OA was not statistically different than NSAIDs. Patients who received tanezumab 2.5 mg did not experience a statistically significant improvement in pain, physical function or patients' overall assessment of their OA at 16 weeks compared to NSAIDs. In the safety analysis, there was a higher rate of joint safety events in the tanezumab arms compared to NSAIDs at 80 weeks; the difference was statistically significant. Joint safety was a composite measure consisting of adjudicated outcomes of rapidly progressive osteoarthritis (RPOA) type 1 or type 2, subchondral insufficiency fracture, osteonecrosis or pathological fracture. Tanezumab is a monoclonal antibody that is part of an investigational class of non-opioid chronic pain medications known as nerve growth factor (NGF) inhibitors.

"We are analyzing these findings in the context of the recent Phase 3 results as we assess potential next steps for tanezumab," said Ken Verburg, tanezumab development team leader, Pfizer Global Product Development. "We plan to review the totality of data

from our clinical development program for tanezumab with regulatory authorities."

"Lilly and Pfizer recognize the significant unmet needs for patients living with osteoarthritis," said Christi Shaw, president, Lilly Bio-Medicines. "We are committed to understanding these results for people who suffer from chronic pain."

In this study, tanezumab 2.5 mg or 5 mg was administered subcutaneously (SC) every eight weeks, for a total of 56 weeks. Preliminary safety data showed that the overall adverse event profile with tanezumab was generally consistent with previous studies of tanezumab in OA, though in this study, discontinuations due to adverse events were higher among those receiving tanezumab compared to NSAIDs during the 56-week treatment period. The study also included a 24-week safety follow-up period, for a total of 80 weeks of observation. There were 10 deaths in the study; nine occurred in the tanezumab treatment arms and one in the NSAID treatment arm. None were considered treatment-related: five occurred during the treatment period and five occurred after the treatment period.

The incidence of the primary composite joint safety endpoint was 7.1 percent in the tanezumab 5 mg arm, 3.8 percent in the tanezumab 2.5 mg arm and 1.5 percent in the NSAIDs arm. RPOA accounted for the majority of events observed in the composite joint safety endpoint. The incidence of RPOA overall was 6.3 percent in the tanezumab 5 mg arm, 3.2 percent in the tanezumab 2.5 mg arm and 1.2 percent in the NSAIDs arm. The majority of RPOA events (81 percent) observed with tanezumab were RPOA type 1. There was one patient with osteonecrosis in the tanezumab 5 mg arm, and no patients in the tanezumab 2.5 mg or NSAIDs arms. Subchondral insufficiency fracture was observed in seven, six and four patients receiving tanezumab 5 mg, tanezumab 2.5 mg and NSAIDs, respectively. There were no pathological fractures observed in patients treated with tanezumab or NSAIDs. The incidence of total joint replacement was 8.0 percent in the tanezumab 5 mg arm, 5.3 percent in the tanezumab 2.5 mg arm and 2.6 percent in the NSAIDs arm.

The full results from this study will be submitted for future scientific publication or presentation.

About the Study

Study A4091058 was a randomized, double-blind, active-controlled, multicenter, parallel-group study evaluating the safety and efficacy of SC administration of tanezumab for 56 weeks compared to NSAIDs in patients with moderate-to-severe OA. The study was conducted worldwide (United States, Europe, Asia and Latin America).

Patients considered for this study had experienced inadequate pain relief from or intolerance to acetaminophen and either tramadol or opioids (or unwilling to take opioids). They were on a stable dose of NSAID before being screened into the study and had experienced at least some benefit from stable NSAID treatment during the period prior to randomization. On average patients had suffered from OA for approximately eight years and had baseline Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain scores of seven out of 10. At the beginning of the study, they also reported a significant impact of their pain on their ability to function in everyday life.

A total of 3,021 patients were randomized in a 1:1:1 ratio to receive either tanezumab 2.5 mg every eight weeks, tanezumab 5 mg every eight weeks, or oral NSAIDs (either naproxen 500 mg, celecoxib 100 mg or diclofenac Extended Release 75 mg) twice daily over the 56-week treatment period. The study also included a 24-week safety follow-up period.

The primary safety endpoint evaluated a composite measure of adjudicated outcomes of RPOA type 1 or type 2, subchondral insufficiency fracture, primary osteonecrosis or pathological fracture through 80 weeks (56 weeks of treatment plus a 24-week safety follow-up period). RPOA type 1 was defined as a significant loss of joint space width ≥2 mm (predicated on optimal joint positioning) within approximately one year, without gross structural failure. RPOA type 2 was defined as abnormal bone loss or destruction, including limited or total collapse of at least one subchondral surface that is not normally present in conventional end-stage OA. The co-primary efficacy endpoints evaluated changes from baseline to week 16 in the WOMAC Pain subscale, the WOMAC Physical Function subscale, and the Patient’s Global Assessment of OA.

About Tanezumab

Tanezumab is an investigational monoclonal antibody that works by selectively targeting, binding to and inhibiting NGF. NGF levels increase in the body as a result of injury, inflammation or in chronic pain states. By inhibiting NGF, tanezumab may help to keep pain signals produced by muscles, skin and organs from reaching the spinal cord and brain. Tanezumab has a novel mechanism that acts in the periphery in a different manner than opioids and other analgesics, including NSAIDs, and in studies to date, tanezumab has not demonstrated a risk of addiction, misuse or dependence.

In June 2017, Pfizer and Lilly announced that the U.S. Food and Drug Administration (FDA) granted Fast Track designation for tanezumab for the treatment of OA and chronic low back pain. Fast Track designation is a process designed to facilitate the development and

expedite the review of new therapies that treat serious conditions and fill unmet medical needs.

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About Eli Lilly and Company

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PFIZER DISCLOSURE NOTICE:

The information contained in this release is as of April 18, 2019. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about a product candidate, tanezumab, including its potential benefits, that involves substantial risks and uncertainties that could

cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, the uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for our clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as the possibility of unfavorable new clinical data and further analyses of existing clinical data; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when drug applications for any potential indications for tanezumab may be filed in any jurisdictions; whether and when regulatory authorities in any jurisdictions may approve any such applications, which will depend on myriad factors, including making a determination as to whether the product's benefits outweigh its known risks and determination of the product's efficacy and, if approved, whether tanezumab will be commercially successful; decisions by regulatory authorities impacting labeling, manufacturing processes, safety and/or other matters that could affect the availability or commercial potential of tanezumab; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2018 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

LILLY DISCLOSURE NOTICE: This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about tanezumab as a potential treatment for patients with osteoarthritis, chronic low back pain, and cancer pain, and reflects Lilly's current beliefs. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of drug development and commercialization. Among other things, there is no guarantee that future study results will be consistent with study findings to date, or that tanezumab will be approved by the U.S. FDA or other regulatory authorities on the anticipated timeline or at all, or that tanezumab will 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.

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