Lilly to Establish an Access Program for Patients as it Prepares to Withdraw Lartruvo from the Global Market

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Lilly is working to ensure current patients access to Lartruvo with limited interruption after it is withdrawn from the market

INDIANAPOLIS, April 25, 2019 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced that the company has been working to facilitate the withdrawal of Lartruvo® (olaratumab) from the market for the treatment of advanced soft tissue sarcoma (STS). Lilly's actions to withdraw Lartruvo from the market follow the failure of the Phase 3 ANNOUNCE clinical trial, in which Lartruvo did not improve survival for patients. Lilly is establishing a program to ensure current patients will have access to Lartruvo with limited interruption after it is withdrawn from the market. The program will be established as allowed by local country regulations.

Lilly is working to ensure that patients who are currently receiving Lartruvo may, in consultation with their physician, continue their course of therapy if they have been informed of the risks of Lartruvo and the results of the ANNOUNCE study and wish to continue, subject to local laws and regulations. No new patients should receive Lartruvo outside of participation in ongoing clinical trials.

Lilly also is working to establish a program to allow patients who are currently receiving Lartruvo to continue treatment with limited interruption after Lartruvo is withdrawn from the market, subject to local laws and regulations. More information regarding this program will be provided directly to healthcare professionals in the coming weeks.

"Lilly wants to ensure that patients and physicians feel supported during this important time," said Anne White, president, Lilly Oncology. "Advanced soft tissue sarcoma is a rare and difficult-to-treat cancer. Establishing this program will give patients who are currently taking Lartruvo the opportunity to continue their treatment program uninterrupted."

Lilly plans to present the ANNOUNCE data at the American Society of Clinical Oncology (ASCO) 2019 annual meeting and will publish the results in a medical journal.

About Soft Tissue Sarcoma
Sarcomas are a diverse and relatively rare type of cancer that usually develop in the connective tissue of the body, which include fat, blood vessels, nerves, bones, muscles, deep skin tissues and cartilage. Soft tissue sarcoma (STS) is a complex disease with multiple subtypes, making it hard to diagnose and difficult to treat. According to the American Cancer Society, in 2019, an estimated 12,750 new STS cases will be diagnosed, and more than 5,000 people will not survive their disease in the U.S. alone. For decades, there have been no first-line therapeutic advancements for STS that have improved overall survival (OS).

About LARTRUVO® (olaratumab)
LARTRUVO is a platelet-derived growth factor receptor alpha (PDGFR-α) blocking antibody that specifically binds PDGFR-α and prevents receptor activation. LARTRUVO exhibits *in vitro* and *in vivo* anti-tumor activity against selected sarcoma cell lines and disrupted the PDGFR-α signaling pathway in *in vivo* tumor implant models.

About the ANNOUNCE Trial
ANNOUNCE was a randomized, double-blind, Phase 3 study of LARTRUVO in combination with doxorubicin, followed by LARTRUVO monotherapy, versus doxorubicin plus placebo followed by placebo, in patients with advanced or metastatic STS. The two primary endpoints were OS in the intent-to-treat (ITT) population and OS in the leiomyosarcoma (LMS) sub-population. Patients with locally advanced, unresectable or metastatic STS not amenable to curative treatment were enrolled and were eligible with any prior number of treatment regimens, provided they had not previously received treatment with an anthracycline.

LARTRUVO was administered at a loading dose of 20 mg/kg on days 1 and 8 of cycle 1 and 15 mg/kg on days 1 and 8 of all subsequent cycles in combination with doxorubicin 75 mg/m^2 administered on day 1 of each cycle. Placebo was administered in combination with doxorubicin for 8 cycles. LARTRUVO was continued as monotherapy until disease progression.

Key secondary endpoints included safety, progression-free survival, objective response rate, and patient-reported outcomes.

INDICATION
LARTRUVO is indicated, in combination with doxorubicin, for the treatment of adult patients with soft tissue sarcoma (STS) with a histologic subtype for which an anthracycline-containing regimen is appropriate and which is not amenable to curative treatment with radiotherapy or surgery.

This indication was approved under Accelerated Approval. Continued approval for this indication was contingent upon verification and description of clinical benefit in the confirmatory trial.

IMPORTANT SAFETY INFORMATION FOR LARTRUVO

Warnings and Precautions

Infusion-Related Reactions

- Infusion-related reactions (IRR) occurred in 70 (14%) of 485 patients who received at least one dose of LARTRUVO across clinical trials. For 68 of these 70 patients (97%), the first occurrence of IRR was in the first or second cycle. Grade ≥3 IRR occurred in 11 (2.3%) of 485 patients, with one (0.2%) fatality. Symptoms of IRR included flushing, shortness of breath, bronchospasm, or fever/chills, and in severe cases symptoms manifested as severe hypotension, anaphylactic shock, or cardiac arrest. Infusion-related reactions required permanent discontinuation in 2.3% of patients and interruption of infusion in 10% of patients. All 59 patients with Grade 1 or 2 IRR resumed LARTRUVO; 12 (20%) of these patients had a Grade 1 or 2 IRR with rechallenge. The incidence of IRR in the overall safety database (N = 485) was similar (18% versus 12%) between those who did (56%) and those who did not (44%) receive premedication. Monitor patients during and following LARTRUVO infusion for signs and symptoms of IRR in a setting with available resuscitation equipment. Immediately and permanently discontinue LARTRUVO for Grade 3 or 4 IRR.

Embryo-Fetal Toxicity

- Based on animal data and its mechanism of action, LARTRUVO can cause fetal harm when administered to a pregnant woman. Animal knockout models link disruption of platelet-derived growth factor receptor alpha (PDGFR-α) signaling to adverse effects on embryo-fetal development. Administration of an anti-murine PDGFR-α antibody to pregnant mice during organogenesis caused malformations and skeletal variations. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with LARTRUVO and for 3 months after the last dose.

Most Common Adverse Reactions/Lab Abnormalities

- The most commonly reported adverse reactions (all grades; grade 3-4) occurring in ≥20% of patients receiving LARTRUVO plus doxorubicin versus doxorubicin alone were nausea (73% vs 52%; 2% vs 3%), fatigue (69% vs 69%; 9% vs 3%), musculoskeletal pain (64% vs 25%; 8% vs 2%), mucositis (53% vs 35%; 3% vs 5%), alopecia (52% vs 40%; 0% vs 0%), vomiting (45% vs 19%; 0% vs 0%), diarrhea (34% vs 23%; 3% vs 0%) decreased appetite (31% vs 20%; 2% vs 0%), abdominal pain (23% vs 14%; 3% vs 0%), neuropathy (22% vs 11%; 0% vs 0%), and headache (20% vs 9%; 0% vs 0%).
- The most common laboratory abnormalities (all grades; grade 3-4) occurring in ≥20% of patients receiving LARTRUVO plus doxorubicin versus doxorubicin alone were lymphopenia (77% vs 73%; 44% vs 37%), neutropenia (65% vs 63%; 48% vs 38%) and thrombocytopenia (63% vs 44%; 6% vs 11%), hyperglycemia (52% vs 28%; 2% vs 3%), elevated aPTT (33% vs 13%; 5% vs 0%), hypokalemia (21% vs 15%; 8% vs 3%), and hypophosphatemia (21% vs 7%; 5% vs 3%).

Use in Specific Populations

- Lactation: Because of the potential risk for serious adverse reactions in breastfeeding infants, advise women not to breastfeed during treatment with LARTRUVO and for at least 3 months following the last dose.

For more information about LARTRUVO, please see full Prescribing Information at http://pi.lilly.com/us/lartruvo-uspi.pdf**.**

About Lilly Oncology
For more than 50 years, Lilly has been dedicated to delivering life-changing medicines and support to people living with cancer and those who care for them. Lilly is determined to build on this heritage and continue making life better for all those affected by cancer around the world. To learn more about Lilly's commitment to people with cancer, please visit www.LillyOncology.com**.**

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 http://newsroom.lilly.com/social-channels. P-LLY

Lilly Forward-Looking Statement
This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about LARTRUVO (olaratumab) as a treatment for patients with advanced soft tissue sarcoma and reflects Lilly's current belief. As with any pharmaceutical product, there are substantial risks and uncertainties in the process of development, commercialization, and in this case, product withdrawal from the market. 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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