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Lilly and Merck Expand Immuno-Oncology Collaboration

New Study to Evaluate Combination of LARTRUVO™ (olaratumab) and KEYTRUDA® (pembrolizumab)

INDIANAPOLIS, Jan. 11, 2017 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced the expansion of an existing immuno-oncology collaboration with Merck, known as MSD outside the U.S. and Canada, through a subsidiary, to add a new study of Lilly's LARTRUVO™ (olaratumab) with KEYTRUDA® (pembrolizumab) in patients with previously treated advanced or metastatic soft tissue sarcoma (STS).

Notably, the U.S. Food and Drug Administration (FDA) recently granted accelerated approval for LARTRUVO (olaratumab injection, 10 mg/mL), in combination with doxorubicin, for the treatment of adults with 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. LARTRUVO (olaratumab injection, 10 mg/mL), in combination with doxorubicin, also recently received conditional marketing authorization from the European Medicines Agency for the treatment of adults with advanced STS not amenable to curative treatment with surgery or radiotherapy and who have not been previously treated with doxorubicin.

"We look forward to further expanding our collaboration with Merck to include this combination study focused on advanced soft tissue sarcoma, a rare and difficult-to-treat disease with limited treatment options," said Sue Mahony, Ph.D., senior vice president and president, Lilly Oncology. "This collaborative study builds on the exciting data we have seen with olaratumab and supports our focus on investigating the potential of rational combinations to enhance efficacy and change the standards of care for people with cancer."

"Historic and present day scientific advances continue to reinforce the role of combination therapies in extending the lives of people with cancer," said Eric Rubin, M.D., vice president and therapeutic area head, oncology early-stage development, Merck Research Laboratories. "Our collaboration with Lilly exemplifies our commitment to fully exploring combination regimens with KEYTRUDA to help arm physicians with the treatment tools they need to help their patients."

Lilly is the sponsor of the Phase 1 study and enrollment is expected to begin mid-2017. Financial details of the collaboration were not disclosed.

In addition to the study announced today, other ongoing trials between Lilly and Merck, through a subsidiary, include:

- Studies of pemetrexed (plus carboplatin) and pembrolizumab in first-line nonsquamous non-small cell lung cancer (NSCLC), including a Phase 3 study that is currently enrolling patients;
- A Phase 1 study examining the combination of ramucirumab with pembrolizumab in NSCLC, gastric cancer and bladder cancer;
- A Phase 1 study examining the combination of necitumumab with pembrolizumab in NSCLC; and
- A Phase 1 study examining the combination of abemaciclib, a CDK 4 and 6 inhibitor, with pembrolizumab. Based on the Phase 1 trial results, the collaboration has the potential to progress to Phase 2 trials in patients who have been diagnosed with either metastatic breast cancer or NSCLC.

Olaratumab (marketed under the brand name 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.

Pembrolizumab (marketed under the brand name KEYTRUDA®) is a humanized monoclonal antibody that works by increasing the ability of the body's immune system to help detect and fight tumor cells. Pembrolizumab blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2, thereby activating T lymphocytes, which may affect both tumor cells and healthy cells.

NOTES TO EDITORS

About Sarcomas

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 is a complex disease with multiple subtypes, making it very hard to diagnose and difficult to treat. For decades, there have been no front-line therapeutic advancements for STS that have improved overall survival. According to the American Cancer Society, in 2015, there were an estimated 12,000 new STS cases diagnosed and nearly 5,000 deaths in the U.S. alone.

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 is approved under Accelerated Approval. Continued approval for this indication may be 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**.**

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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 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 newsroom.lilly.com/social-channels. **P-LLY**

KEYTRUDA® is a registered trademark of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.

Lilly Forward-Looking Statement
This press release contains "forward-looking statements" (as that term is defined in the United States Private Securities Litigation Reform Act of 1995) regarding the research collaborations between Lilly and Merck evaluating LARTRUVO (olaratumab) with KEYTRUDA (pembrolizumab), pemetrexed (plus carboplatin) and pembrolizumab, ramucirumab with pembrolizumab, necitumumab with pembrolizumab, and abemaciclib with pembrolizumab, and reflects Lilly's current beliefs. However, there are substantial risks and uncertainties in the process of drug research, development and commercialization. Among other risks, there can be no guarantee that these investigational combination regimens will receive regulatory approval, or, if approved, will achieve intended benefits or become commercially successful. For further discussion of these and other risks and uncertainties that could cause actual results to differ materially from Lilly's expectations, please see the company's latest Forms 10-K and 10-Q filed with the U.S. Securities and Exchange Commission. Except as required by law, Lilly undertakes no duty to update forward-looking statements for events occurring after the date of this release.

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