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Lilly Builds Upon Body of Data for Abemaciclib with Phase 3 MONARCH 2 Data Demonstrating Superior Progression-Free Survival in Advanced Breast Cancer

- **Abemaciclib plus fulvestrant significantly improved efficacy outcomes over placebo plus fulvestrant**
- **Data presented at the 2017 Annual Meeting of the American Society of Clinical Oncology (ASCO) and published in the Journal of Clinical Oncology**
- **Lilly announces initiation of monarchE - a global Phase 3 study of abemaciclib as adjuvant therapy in early breast cancer**

INDIANAPOLIS, June 3, 2017 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced that results from the Phase 3 MONARCH 2 study showed that abemaciclib, a cyclin-dependent kinase (CDK)4 & 6 inhibitor, in combination with fulvestrant, significantly improved progression-free survival (PFS) compared to treatment with fulvestrant alone in women with hormone-receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-), advanced breast cancer who have relapsed or progressed after endocrine therapy (median PFS, 16.4 vs. 9.3 months, respectively, HR: 0.553; 95% CI: 0.449, 0.681, $P < .0000001$). The data were presented at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting (Abstract #1000) and simultaneously published online in the *Journal of Clinical Oncology*.

"Metastatic HR+ breast cancer remains a dangerous disease and oncologists are always on the lookout for active new therapies to combat it," said George W. Sledge Jr., M.D., professor of medicine, Stanford University School of Medicine and principal investigator. "I am very impressed with the results from this study. For these patients who progressed on endocrine therapy, there was a significant prolongation of progression-free survival, and more than double the response rate, including an increased rate of complete response."

Patients with measureable disease treated with abemaciclib plus fulvestrant achieved an objective response rate (ORR) of 48.1 percent (3.5% complete response [CR]), compared to 21.3 percent (0% CR) in patients treated with fulvestrant alone. Additionally, abemaciclib plus fulvestrant caused a greater degree of tumor shrinkage than fulvestrant alone.

"One of our goals with the MONARCH clinical development program is not to replicate studies, but rather to further innovate in the field of CDK4 & 6 inhibition and advance potential treatment options for patients wherever they may be in the course of their disease," said Levi Garraway, M.D., Ph.D., senior vice president, global development and medical affairs, Lilly Oncology. "From the single-agent activity seen in MONARCH 1 to the significant MONARCH 2 results shared today, and our ongoing Phase 3 studies, we are committed to working with physicians to evolve treatment expectations for people living with breast cancer."

The global Phase 3, double-blind study was designed to evaluate the efficacy and safety of abemaciclib, in combination with fulvestrant, in patients with advanced (locoregionally recurrent or metastatic) breast cancer. The intent-to-treat population of 669 patients was randomized to receive abemaciclib or placebo orally twice a day on a continuous dosing schedule, given in combination with fulvestrant at its approved dose and schedule, until disease progression. Patients enrolled in the study had experienced disease progression on or within 12 months of receiving endocrine treatment in the neoadjuvant or adjuvant setting or while receiving first-line endocrine therapy for metastatic disease. Patients who had received chemotherapy in the metastatic setting were not eligible for the study. The primary endpoint for MONARCH 2 was PFS.

The most frequent adverse events (AEs) of any grade in the abemaciclib plus fulvestrant arm were diarrhea, neutropenia, nausea, and fatigue. Of these, the reported Grade 3 AEs (abemaciclib vs. placebo arm) were diarrhea (13.4% vs. 0.4%), neutropenia (23.6% vs. 1.3%), nausea (2.7% vs. 0.9%), and fatigue (2.7% vs. 0.4%). No patients in either arm experienced Grade 4 diarrhea, nausea or fatigue, and Grade 4 neutropenia was observed in 2.9 percent versus 0.4 percent of patients in the abemaciclib versus placebo arms, respectively.

Severity and frequency of diarrhea generally decreased following one to two cycles, and was managed with loperamide or dose reduction. The majority (70.1%) of patients in the abemaciclib arm with an AE of diarrhea did not require treatment modification (dose interruption, reduction, or discontinuation), and 2.9 percent of patients discontinued the study drug due to diarrhea.

In addition to the ongoing MONARCH trials, including the newly initiated monarchE adjuvant study, which will assess

abemaciclib in patients with high-risk, early breast cancer, Lilly is actively evaluating abemaciclib in lung cancer, pancreatic cancer, and patients with brain metastases.

Notes to Editor

About Advanced Breast Cancer

Breast cancer is the most common cancer in women worldwide with nearly 1.7 million new cases diagnosed in 2012.^[1] Advanced breast cancer includes metastatic breast cancer, cancer that has spread from the breast tissue to other parts of the body, and locally or regionally advanced breast cancer, meaning the cancer has grown outside the organ where it started but has not yet spread to other parts of the body.^[2] Of all early stage breast cancer cases diagnosed in the U.S., approximately 30 percent will become metastatic and an estimated six to 10 percent of all new breast cancer cases are initially diagnosed as being metastatic.^[3] Survival is lower among women with a more advanced stage at diagnosis: 5-year relative survival is 99 percent for localized disease, 85 percent for regional disease, and 26 percent for metastatic disease. Other factors, such as tumor size, also impact 5-year survival estimates.^[4]

About Abemaciclib

In many cancers, uncontrolled cell growth arises from a loss of cell cycle regulation due to increased signaling from CDK4 and CDK6. Abemaciclib (LY2835219) is an investigational, oral cell cycle inhibitor, designed to block the growth of cancer cells by specifically inhibiting cyclin-dependent kinases, CDK4 and CDK6, and was most active against Cyclin D1 and CDK4 in cell-free enzymatic assays. In breast cancer, Cyclin D1/CDK4 has been shown to promote phosphorylation of the retinoblastoma protein (Rb), cell proliferation and tumor growth. In hormone receptor-positive breast cancer cell lines, sustained target inhibition by abemaciclib reduced phosphorylation of Rb, inducing cell cycle arrest.

In 2015, the U.S. Food and Drug Administration granted abemaciclib Breakthrough Therapy Designation based on data from the breast cancer cohort expansion of the company's Phase 1 trial, JPBA, which studied the efficacy and safety of abemaciclib in women with advanced or metastatic breast cancer. In addition to its current MONARCH clinical trials evaluating abemaciclib in breast cancer, a Phase 3 trial of abemaciclib in lung cancer is also underway.

For more information on additional abemaciclib trials, a complete listing can be found on [ClinicalTrials.gov](https://clinicaltrials.gov) (in the search box on the home page, type in "abemaciclib").

About the MONARCH Clinical Trial Program

Lilly is evaluating abemaciclib in the comprehensive MONARCH clinical program, which includes the following studies:

MONARCH 1: a global Phase 2 study evaluating the efficacy and safety of abemaciclib monotherapy in patients with HR+, HER2- advanced breast cancer who had prior endocrine therapy and chemotherapy for metastatic disease.

MONARCH 2: a global Phase 3 study evaluating the efficacy and safety of abemaciclib, in combination with fulvestrant, in patients with HR+, HER2- advanced breast cancer who progressed on endocrine therapy.

MONARCH 3: a global Phase 3 study evaluating the efficacy and safety of abemaciclib, in combination with an aromatase inhibitor, as initial endocrine-based therapy for postmenopausal women with HR+, HER2- advanced breast cancer who have had no prior systemic treatment for advanced disease.

monarchHER: a global Phase 2 study evaluating abemaciclib plus trastuzumab (with or without fulvestrant) in women with HR+, HER2+ advanced breast cancer.

MONARCH plus: a Phase 3 study evaluating the efficacy and safety of abemaciclib, in combination with endocrine therapies, to support registration in China.

neoMONARCH: a Phase 2 study evaluating abemaciclib in the neoadjuvant setting, alone or in combination with the non-steroidal aromatase-inhibitor anastrozole, in postmenopausal women with previously untreated early stage HR+, HER2- breast cancer.

monarchE: a global Phase 3 study evaluating the efficacy and safety of abemaciclib in the adjuvant setting in patients with high-risk, early breast cancer.

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

Fulvestrant (Faslodex[®]), MedImmune/AstraZeneca. MedImmune Limited/AstraZeneca provided fulvestrant for this trial.

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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 abemaciclib as a potential treatment for patients with breast cancer and reflects Lilly's current beliefs. 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 abemaciclib will receive 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.

[1] World Cancer Research Fund International. Breast Cancer. http://www.wcrf.org/cancer_statistics/data_specific_cancers/breast_cancer_statistics.php. Accessed: May 17, 2017.

[2] American Cancer Society. Understanding Advanced Cancer, Metastatic Cancer and Bone Metastases. <https://www.cancer.org/treatment/understanding-your-diagnosis/advanced-cancer/what-is.html>. Accessed: May 17, 2017.

[3] Metastatic Breast Cancer Network. 13 Facts about Metastatic Breast Cancer. <http://www.mbcn.org/13-facts-about-metastatic-breast-cancer/>. Accessed: May 17, 2017.

[4] American Cancer Society. Breast Cancer Facts & Figures 2015-2016. <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/breast-cancer-facts-and-figures/breast-cancer-facts-and-figures-2015-2016.pdf>. Accessed: May 17, 2017.

Refer to: Erin Graves; graves_erin_elissa@lilly.com; 908-202-6354 (media)
Phil Johnson; johnson_philip_l@lilly.com; 317-655-6874 (investors)



To view the original version on PR Newswire, visit: <http://www.prnewswire.com/news-releases/lilly-builds-upon-body-of-data-for-abemaciclib-with-phase-3-monarch-2-data-demonstrating-superior-progression-free-survival-in-advanced-breast-cancer-300468289.html>

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