Press Release

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Pfizer Japan Inc.

National Cancer Center Hospital and Pfizer Japan, in a New Collaboration Framework, Announce Positive Top-Line Results from PATHWAY, a Phase III Study Evaluating Palbociclib Plus Tamoxifen in Patients with Hormone Receptor-positive, HER2-negative Advanced Breast Cancer

Pfizer Japan Inc. (Head Office: Shibuya-ku, Tokyo; President: Akihisa Harada) announced today the positive topline results of the randomized Phase III study [PATHWAY] of palbociclib (product name: IBRANCE®) in combination with tamoxifen in pre/post-menopausal women with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) advanced or metastatic breast cancer; the study met its primary endpoint improving progression-free survival (PFS).

PATHWAY is an Asian, international, multicenter, randomized, double-blind, Phase III study that compares palbociclib plus tamoxifen with placebo plus tamoxifen in pre/postmenopausal patients with HR+/HER2- advanced or metastasis breast cancer. This study is an international clinical trial sponsored by National Cancer Center Hospital that has been conducted as part of a Clinical Research Collaboration (hereinafter referred to as the "CRC") with Asian academia and Pfizer (providing study drug and funding), which is a new collaboration framework in Japan[1].

Researchers in academia have developed and established their own clinical study organizations which have been actively conducting investigator-initiated clinical trials, especially in the US and Europe. Recently, laws and regulations on investigator-initiated clinical trials have been established in Japan as well, offering opportunities for new treatment strategies developed by researchers/research groups and pharmaceutical companies.

As a result of these new laws and regulations, a CRC collaboration framework was recently made available to enable pharmaceutical companies in Japan to generate relevant and important clinical data related to novel treatments through partnership with researchers/research groups. CRC studies are sponsored by a researcher(s) or research group(s), responsible for the conduct and execution of the trials in accordance with regulatory requirements and the study protocol. Under

this framework, pharmaceutical companies are involved in the design and planning of the trial as well as have an oversight of the conduct of the clinical trials and provide study drug and/or funding.

The study met its primary endpoint by demonstrating a statistically significant and clinically meaningful improvement in PFS for the combination of palbociclib and tamoxifen compared with tamoxifen alone in pre/post-menopausal women with HR+/HER2- advanced or metastatic breast cancer. Although overall survival (OS) data were immature at the time of the analysis, early data are encouraging. The trial will continue to assess OS and will be reported at a later timepoint.

The safety and efficacy of this combination has not previously been established in this investigational use. In the PATHWAY study, the combination therapy was well tolerated, and the safety profile was consistent with the overall safety profile seen in other clinical trials investigating palbociclib in combination with endocrine therapies. Detailed efficacy and safety data from PATHWAY study will be presented at an upcoming scientific meeting.

[Comments of Taro Ishibashi, President of Pfizer R&D Japan G. K.]
"Tamoxifen has been widely used as first-line treatment mainly for pre/postmenopausal patients with advanced breast cancer and as second or greater line treatment for postmenopausal patients with advanced breast cancer, but the efficacy of palbociclib in combination with tamoxifen had not been studied in a large phase III study.

We are pleased that the PATHWAY study, conducted as a collaboration between academia and industry, has met its primary objective and believe that the study demonstrated important results that showed the addition of palbociclib to tamoxifen provides clinical benefit over tamoxifen alone in patients with HR+/HER2- advanced or metastasis breast cancer.

We will continue to explore opportunities to use the CRC framework to support future registrational activities in Japan."

About PATHWAY

■ **Study design**

PATHWAY is an Asian, international, multicenter, randomized, double-blind, Phase III study

in pre/postmenopausal patients with HR+/HER2- advanced or metastasis breast cancer.
A total of 184 patients were randomized 1:1 to receive palbociclib plus tamoxifen or placebo plus tamoxifen, and the efficacy and safety of palbociclib in combination with tamoxifen were evaluated with the primary endpoint of PFS based on investigator assessment. Patients received palbociclib 125 mg/day or placebo, orally once daily on Day 1 to Day 21 followed by 7 days off treatment for each 28-day cycle and tamoxifen 20 mg orally once daily (continuously). Pre- and peri-menopausal patients received LH-RH agonists (goserelin).

PATHWAY is sponsored by the National Cancer Center Hospital, and was conducted in 4 countries: Japan (12 centers), South Korea (6 centers), Taiwan (3 centers), and Singapore (2 centers).

About Palbociclib (product name: IBRANCE ®)

Palbociclib is an oral molecular target drug that inhibits CDK4/6[2]. CDK4/6 plays a primary role in regulating the cell cycle, causing cellular proliferation. It is believed that palbociclib suppresses the proliferation of tumors by selectively inhibiting CDK4/6 and arresting the progression of cell cycle[3,4]. Palbociclib efficacy and acceptable toxicities were demonstrated in a global phase III study of palbociclib plus letrozole versus placebo plus letrozole in postmenopausal women with estrogen receptor (ER)+ /HER2- advanced breast cancer who have not received any prior systemic anti-cancer therapy for their advanced disease (PALOMA-2) and in a global phase III study of palbociclib plus fulvestrant ± goserelin versus placebo plus fulvestrant ± goserelin in pre/postmenopausal women with HR+/HER2- advanced breast cancer whose disease progressed after prior endocrine therapy (PALOMA-3).
Palbociclib has been approved in more than 100 countries worldwide. In Japan, based on the results of PALOMA-2 and PALOMA-3, palbociclib 25 mg and 125 mg capsules and tablets (Brand name: IBRANCE capsules 25 mg, 125 mg, and IBRANCE tablets 25 mg, 125 mg) were approved for the indication of "hormone receptor-positive and HER2-negative, inoperable or recurrent breast cancer" on 27 September 2017 and 23 January 2020, respectively.
※IBRANCE (generic name: palbociclib) in combination with tamoxifen is not approved. For details, refer to the latest package insert.

About “Learning Breast Cancer”

Since its opening in 2012, our comprehensive cancer information site “Learning About Cancer” for cancer patients and their families has boasted the highest number of accesses in the

pharmaceutical industry. One of the sites, "Learning Breast Cancer," provides easy-to-understand explanations of breast cancer symptoms, screening methods, and treatment methods such as surgery, radiotherapy, and drug therapy. https://ganclass.jp/kind/breast/

About My Choice Program

"I want to make better choices in order to continue with my current lifestyle." We have posted evidence-based medical information and financial systems so that each person can make their own choices and live with metastatic and recurrent breast cancer every day. Incorporating the voices of breast cancer patients, this program will be developed for Japanese patients, and we will continue to be close to patients and their families.
https://mychoiceprogram.jp/index.html#home

<Reference>

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2. IBRANCE® (palbociclib) Prescribing Information. New York. NY: Pfizer Inc: 2022.
3. Weinberg, RA. pRb and Control of the Cell Cycle Clock. In: Weinberg RA, ed. The Biology of Cancer. 2nd ed. New York, NY: Garland Science; 2014:275-329.
4. Sotillo E, Grana X. Escape from Cellular Quiescence. In: Enders GH, ed. Cell Cycle Deregulation in Cancer. New York, NY: Humana Press; 2010:3-22.

About Pfizer Oncology

At Pfizer Oncology, we are committed to advancing medicines wherever we believe we can make a meaningful difference in the lives of people living with cancer. Today, we have an industry-leading portfolio of 24 approved innovative cancer medicines and biosimilars across more than 30 indications, including breast, genitourinary, colorectal, blood and lung cancers, as well as melanoma.

About Pfizer: Breakthroughs That Change Patients' Lives

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products, including innovative medicines and vaccines. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative

biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 170 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.Pfizer.com. In addition, to learn more, please visit us on www.Pfizer.com and follow us on Twitter at @Pfizer and @Pfizer News, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.