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MEDIA & INVESTOR RELEASE

Novartis Piqray® receives positive CHMP opinion to treat HR+/HER2- advanced breast cancer with a PIK3CA mutation

- *Piqray (alpelisib) in combination with fulvestrant will become first and only targeted treatment for advanced breast cancer patients whose tumors harbor a PIK3CA mutation in Europe*

- *Phase III trial showed Piqray plus fulvestrant nearly doubled median PFS (11.0 vs. 5.7 months) in this patient population, compared to fulvestrant alone*

- *PIK3CA mutations affect approximately 40% of HR+/HER2- advanced breast cancer patients and are linked to cancer growth and a poorer disease prognosis in the metastatic setting*

Basel, May 29, 2020 — Novartis today announced the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency has adopted a positive opinion recommending approval of Piqray® (alpelisib) in combination with fulvestrant for the treatment of postmenopausal women, and men, with hormone receptor positive, human epidermal growth factor receptor-2 negative (HR+/HER2-) locally advanced or metastatic breast cancer with a PIK3CA mutation after disease progression following endocrine therapy as monotherapy.

“PIK3CA is the most commonly mutated gene in HR+/HER2- advanced breast cancer, affecting approximately 40% of patients. If approved, alpelisib has the potential to transform the way we treat this cancer in Europe, offering physicians a clear treatment for patients with a PIK3CA mutation that nearly doubles the time to disease progression,” said Fabrice André, MD, PhD, research director and head of INSERM Unit U981, professor in the Department of Medical Oncology at Institut Gustave Roussy in Villejuif, France, and global SOLAR-1 principal investigator.

The CHMP opinion is based on results of the Phase III SOLAR-1 trial that showed Piqray plus fulvestrant nearly doubled median progression-free survival (PFS) compared to fulvestrant alone in HR+/HER2- advanced breast cancer patients with tumors harboring a PIK3CA mutation (median PFS 11.0 months vs. 5.7 months; HR=0.65, 95% CI: 0.50-0.85; p<0.001), the study’s primary endpoint. PFS subgroup analyses demonstrated consistent efficacy in favor of Piqray, irrespective of presence or absence of lung/liver metastases.

“We are excited about today’s CHMP opinion, recommending the first and only treatment option for European patients specifically developed to target the PIK3CA mutation in their cancer,” said Susanne Schaffert, PhD, President, Novartis Oncology. “Piqray is another

example of how we are reimagining cancer care to bring new targeted therapies to patients with high unmet needs that help them live longer without disease progression."

In SOLAR-1, most adverse events were mild to moderate in severity and generally manageable through dose modifications and medical management. Of these, the most common grade 3/4 events (≥7%) were plasma glucose increased (39.1%), rash (19.4%), gamma-glutamyltransferase increased (12.0%), lymphocyte count decreased (9.2%), diarrhea (7.0%) and lipase increased (7.0%). No patients developed diabetes as a result of transient hyperglycemia.

The European Commission will review the CHMP recommendation and usually delivers a final decision within approximately two months. The decision will be applicable to all 27 European Union member states plus the United Kingdom, Iceland, Norway and Liechtenstein. Additional regulatory filings are underway with other health authorities worldwide.

Patients with HR+/HER2- advanced breast cancer should be selected for treatment with Piqray based on the presence of a PIK3CA mutation in tumor or plasma specimens, using a validated test. If a mutation is not detected in a plasma specimen, tumor tissue should be tested if available.

About Piqray® (alpelisib)
Piqray is a kinase inhibitor developed for use in combination with fulvestrant for the treatment of postmenopausal women, and men, with HR+/HER2-, PIK3CA-mutated, advanced or metastatic breast cancer, as detected by a validated test following progression on or after endocrine-based regimen. Piqray is approved in the U.S., and 12 other countries around the world.

About SOLAR-1
SOLAR-1 is a global, Phase III randomized, double-blind, placebo-controlled trial studying Piqray in combination with fulvestrant for postmenopausal women, and men, with PIK3CA-mutated HR+/HER2- advanced or metastatic breast cancer that progressed on or following aromatase inhibitor treatment with or without a CDK4/6 inhibitor[1,2,3].

The trial randomized 572 patients. Patients were allocated based on central tumor tissue assessment to either a PIK3CA-mutated cohort (n=341) or a PIK3CA non-mutated cohort (n=231). Within each cohort, patients were randomized in a 1:1 ratio to receive continuous oral treatment with Piqray (300 mg once daily) plus fulvestrant (500 mg every 28 days + Cycle 1 Day 15) or placebo plus fulvestrant. Stratification was based on visceral metastases and prior CDK4/6 inhibitor treatment[1,2,3]. Patients and investigators are blinded to PIK3CA mutation status and treatment.

The primary endpoint is local investigator assessed PFS using RECIST 1.1 for patients with a PIK3CA mutation. The key secondary endpoint is overall survival, and additional secondary endpoints include, but are not limited to, overall response rate, clinical benefit rate, health-related quality of life, efficacy in PIK3CA non-mutated cohort, safety and tolerability[1,2,3]. SOLAR-1 is ongoing to assess overall survival and other secondary endpoints.

Piqray® (alpelisib) Important Safety Information from the U.S. Prescribing Information
Patients should not take PIQRAY if they have had a severe allergic reaction to PIQRAY or are allergic to any of the ingredients in PIQRAY.

PIQRAY may cause serious side effects. PIQRAY can cause severe allergic reactions. Patients should tell their health care provider or get medical help right away if they have trouble breathing, flushing, rash, fever, or fast heart rate during treatment with PIQRAY. PIQRAY can cause severe skin reactions. Patients should tell their health care provider or get medical help right away if they get severe rash or rash that keeps getting worse, reddened skin, flu-like symptoms, blistering of the lips, eyes or mouth, blisters on the skin or skin

peeling, with or without fever. PIQRAY can cause high blood sugar levels (hyperglycemia). Hyperglycemia is common with PIQRAY and can be severe. Health care providers will monitor patients' blood sugar levels before they start and during treatment with PIQRAY. Health care providers may monitor patients' blood sugar levels more often if they have a history of Type 2 diabetes. Patients should tell their health care provider right away if they develop symptoms of hyperglycemia, including excessive thirst, dry mouth, urinate more often than usual or have a higher amount of urine than normal, or increased appetite with weight loss. PIQRAY can cause lung problems (pneumonitis). Patients should tell their health care provider right away if they develop new or worsening symptoms of lung problems, including shortness of breath or trouble breathing, cough, or chest pain. Diarrhea is common with PIQRAY and can be severe. Severe diarrhea can lead to the loss of too much body water (dehydration) and kidney problems. Patients who develop diarrhea during treatment with PIQRAY should tell their health care provider right away.

Before taking PIQRAY, patients should tell their health care provider if they have a history of diabetes, skin rash, redness of skin, blistering of the lips, eyes or mouth, or skin peeling, are pregnant, or plan to become pregnant as PIQRAY can harm their unborn baby. Females who are able to become pregnant should use effective birth control during treatment with PIQRAY and for 1 week after the last dose. Do not breastfeed during treatment with PIQRAY and for 1 week after the last dose. Males with female partners who are able to become pregnant should use condoms and effective birth control during treatment with PIQRAY and for 1 week after the last dose. Patients should also read the Full Prescribing Information of fulvestrant for important pregnancy, contraception, infertility, and lactation information.

Patients should tell their health care provider all of the medicines they take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. PIQRAY and other medicines may affect each other causing side effects. Know the medicines you take. Keep a list of them to show your health care provider or pharmacist when you get a new medicine.

The most common side effects of PIQRAY when used with fulvestrant are rash, nausea, tiredness and weakness, decreased appetite, mouth sores, vomiting, weight loss, hair loss, and changes in certain blood tests.

Please see full U.S. Prescribing Information for Piqray, available at https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/piqray.pdf.

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pressures and requirements for increased pricing transparency; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; general political, economic and business conditions, including the effects of and efforts to mitigate pandemic diseases such as COVID-19; safety, quality, data integrity or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

About Novartis
Novartis is reimagining medicine to improve and extend people's lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world's top companies investing in research and development. Novartis products reach nearly 800 million people globally and we are finding innovative ways to expand access to our latest treatments. About 109,000 people of more than 145 nationalities work at Novartis around the world. Find out more at https://www.novartis.com.

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