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MEDIA & INVESTOR RELEASE

Novartis Piqray® data show survival benefit for patients with HR+/HER2- advanced breast cancer with a PIK3CA mutation

- *In SOLAR-1 final analysis, Piqray (alpelisib) plus fulvestrant demonstrated 8 months clinically relevant improvement in overall survival (OS) in HR+/HER2- advanced breast cancer (aBC) patients with a PIK3CA mutation compared to fulvestrant alone*[1]

- *14+ months OS improvement was achieved in patients with lung or liver metastases, which are observed in 41% of postmenopausal women with HR+ aBC, and considered more aggressive and challenging to treat*[1-3]

- *Data add to growing body of evidence for Piqray, the first and only treatment specifically approved for aBC with a PIK3CA mutation*

Basel, September 19, 2020 — Novartis today announced results of the final overall survival (OS) analysis from the SOLAR-1 trial, which evaluated Piqray® (alpelisib) in combination with fulvestrant, compared to fulvestrant alone, in hormone receptor positive, human epidermal growth factor receptor-2 negative (HR+/HER2-) advanced breast cancer patients with tumors harboring a PIK3CA mutation. Piqray is the only treatment approved in Europe, the United States and 15 other countries specifically for people with HR+/HER2- advanced breast cancer with a PIK3CA mutation. These data will be presented as a late-breaking oral presentation during the ESMO Virtual Congress 2020.

In the study, there was a clinically relevant improvement in OS of eight months for patients with a PIK3CA mutation taking Piqray plus fulvestrant compared to fulvestrant alone (median OS 39.3 months vs. 31.4 months; one-sided p≤0.0161; HR=0.86; 95% CI: 0.64-1.15; p=0.15)[1]. This difference did not reach the prespecified threshold of statistical significance set for the secondary objective of OS in patients with PIK3CA-mutated breast cancer. A more than 14 month OS improvement was observed in patients with lung or liver metastases, which signify more aggressive disease (median OS 37.2 months vs. 22.8 months; HR=0.68; 95% CI: 0.46-1.00)[1-3].

“These results build on previous data showing that alpelisib nearly doubled median progression-free survival in this patient population,” 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. “Patients whose tumors have a PIK3CA mutation, particularly those with lung or liver metastases, have a more aggressive, harder to treat cancer, so these results showing alpelisib offers longer life, are promising.”

In addition, data showed the need for chemotherapy was delayed in patients taking Piqray plus fulvestrant by nine months compared to those taking fulvestrant alone (23.3 months vs. 14.8 months; HR=0.72; 95% CI: 0.54-0.95)[1]. Quality of life (QOL) was maintained for people taking Piqray plus fulvestrant.

“These data demonstrating survival benefit give the 40% of HR+/HER2- advanced breast cancer patients with PIK3CA mutations in their tumors more time to spend with loved ones and do what they value most,” said Susanne Schaffert, PhD, President, Novartis Oncology. “We are committed to reimagining a world where advanced breast cancer becomes a curable disease, and these data reinforce our confidence as we continue to explore the potential use of Piqray in other types of breast cancer with PIK3CA mutations.”

No new safety signals were observed; adverse events were consistent with previously reported SOLAR-1 results.

Visit https://www.virtualcongress.novartis.com/ESMO20 for the latest information from Novartis including our bold approach to reimagining cancer care, and access to our ESMO Virtual Congress 2020 symposia and data presentations (for registered participants).

In July 2020, the European Commission (EC) approved Piqray in combination with fulvestrant for the treatment of postmenopausal women, and men, with HR+/HER2- locally advanced or metastatic breast cancer with a PIK3CA mutation after disease progression following endocrine therapy as monotherapy.

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 following progression on or after endocrine-based regimen. Piqray is approved in 48 countries, including the US and European member states.

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[7-9].

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[7-9]. 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[7-9].

About Novartis in Advanced Breast Cancer
Novartis tackles breast cancer with superior science, collaboration and a passion for transforming patient care. We've taken a bold approach to our research by including patient populations often neglected in clinical trials, identifying new pathways or mutations that may play a role in disease progression and developing therapies that not only maintain, but also improve, quality of life for patients. Our priority over the past 30 years and today is to deliver treatments proven to improve and extend lives for those diagnosed with advanced breast cancer.

Important Safety Information from the PIQRAY EU SmPC
The most common ADRs and the most common grade 3 / 4 ADRs (reported at a frequency >20% and ≥2%, respectively) were plasma glucose increased, creatinine increased, gamma-glutamyltransferase increased, rash, lymphocyte count decreased, nausea, alanine aminotransferase increased, anaemia, fatigue, lipase increased, decreased appetite*, stomatitis, vomiting*, weight decreased, hypocalcaemia, plasma glucose decreased*, activated partial thromboplastin time prolonged*, alopecia**, diarrhoea, hypokalaemia, hypertension, nausea, creatinine increased, and mucosal inflammation (*<2% grade 3/4 ADRs reported, ** no grade 3/4 ADRs reported).

Piqray can cause serious side effects such as severe hypersensitivity, severe cutaneous reactions, hyperglycaemia, pneumonitis, diarrhoea and osteonecrosis of the jaw.

The following should be taken into consideration prior to or during treatment with Piqray:

Piqray should be permanently discontinued in patients with serious hypersensitivity reactions.

Piqray should not be initiated in patients with a history of severe cutaneous reactions, should be interrupted if signs or symptoms of severe cutaneous reactions are present, and permanently discontinued if a severe cutaneous reaction is confirmed.

Fasting glucose and HbA1c levels should be monitored frequently in the first 4 weeks of treatment, and patients should be advised of the signs and symptoms of hyperglycaemia.

In case of new or worsening respiratory symptoms, the patient should be evaluated for pneumonitis.

Patients should be advised to notify their physician if diarrhoea occurs.

Caution should be exercised when Piqray and bisphosphonates or denosumab are used together or sequentially. Piqray should not be initiated in patients with ongoing osteonecrosis of the jaw.

The efficacy and safety of Piqray has not been studied in patients with symptomatic visceral disease.

Animal studies suggest that Piqray may cause fetal harm in pregnant women. Therefore, as a precaution, women of childbearing potential should use effective contraception while receiving Piqray during treatment and at least 1 week after stopping treatment. Women should not breast feed for at least 1 week after the last dose of Piqray. Piqray may affect fertility in males and females.

Please see full Prescribing Information for Piqray, available at **www.Piqray.com.**

Disclaimer
This press release contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements can generally be identified by words such as “potential,” “can,” “will,” “plan,” “may,” “could,” “would,” “expect,” “anticipate,” “seek,” “look forward,” “believe,” “committed,” “investigational,” “pipeline,” “launch,” or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for the investigational or approved products described in this press release, or regarding potential future revenues from such products. You should not place undue reliance on these statements. Such forward-looking statements are based on our current beliefs and expectations regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results

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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 140 nationalities work at Novartis around the world. Find out more at **https://www.novartis.com**.

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