Novartis International AG
Novartis Global Communications
CH-4002 Basel
Switzerland

https://www.novartis.com
https://twitter.com/novartisnews

MEDIA UPDATE

Novartis receives Piqray® approval in Europe – the first and only targeted medicine for HR+/HER2- advanced breast cancer with a PIK3CA mutation

- *Piqray (alpelisib) is the only treatment approved specifically to address PIK3CA mutation, underscoring Novartis commitment to reimagining cancer care*
- *Approval based on SOLAR-1 Phase III trial showing Piqray plus fulvestrant nearly doubled median PFS (11.0 vs. 5.7 months), compared to fulvestrant alone*[1,2]
- *334,000 people are diagnosed with advanced breast cancer worldwide each year, and approximately 40% of those with HR+/HER2- subtype have a PIK3CA mutation, which is associated with a poor prognosis*[3-12]

Basel, July 29, 2020 — Novartis today announced the European Commission (EC) has approved 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. Piqray is the first and only treatment specifically approved for people with advanced breast cancer whose tumors harbor a PIK3CA mutation, which stimulates tumor growth and is associated with poor response to therapy[13].

“Piqray is an important new therapy for HR+/HER2- advanced breast cancer patients whose tumors have a PIK3CA mutation, and we look forward to making it available in countries across Europe,” said Kees Roks, Head Region Europe, Novartis Oncology. “Knowledge of PIK3CA status can better equip doctors as they develop a personalized upfront treatment plan for patients. Piqray offers new hope for advanced breast cancer patients with a PIK3CA mutation, who typically face a worse overall prognosis.”

This approval follows a positive opinion granted in May by the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) based on the Phase III SOLAR-1 trial showing that Piqray nearly doubled median progression-free survival (PFS) compared to fulvestrant alone[1,2]. Overall response rate, an indicator of the proportion of patients who experience at least a 30% reduction in overall tumor size (in patients with measurable disease), was more than doubled when Piqray was added to fulvestrant compared to fulvestrant alone[1,2]. Read more about the positive CHMP opinion and the SOLAR-1 clinical trial results here.

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

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 download full Summary of Product Characteristics for Piqray here.

Disclaimer
This media update 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 media update, 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 may vary materially from those set forth in the forward-looking statements. There can be no guarantee that the investigational or approved products described in this media update will be submitted or approved for sale or for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that such products will be commercially successful in the future. In particular, our expectations regarding such products could be affected by, among other things, the uncertainties inherent in research and development, including clinical trial results and additional analysis of existing clinical data; regulatory actions or delays or government regulation generally; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement 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 media update as of this date and does not undertake any obligation to update any forward-looking statements contained in this media update 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 140 nationalities work at Novartis around the world. Find out more at https://www.novartis.com.

Novartis is on Twitter. Sign up to follow @Novartis at **https://twitter.com/novartisnews**
For Novartis multimedia content, please visit **https://www.novartis.com/news/media-library**
For questions about the site or required registration, please contact media.relations@novartis.com

References

1. Piqray (alpelisib) Prescribing Information. East Hanover, New Jersey, USA: Novartis Pharmaceuticals Corporation; May 2019.
2. André F, Ciruelos E, Rubovszky G. Alpelisib for PIK3CA-Mutated, Hormone-Receptor-Positive Advanced Breast Cancer. N Eng J Med 2019.
3. Globocan 2018 (WHO), Cancer Today: Estimated number of new cases in 2018, worldwide, females, all ages_1_ 2018.
4. Gheorghe D. Breast Cancer. Decision Resources. July 2017:1-338.
5. Tolaney S, Toi M, Neven P, et al. Presented at: 2019 American Association for Cancer Research (AACR) Annual Meeting; March 29-April 3, 2019; Atlanta, GA.
6. Di Leo A, Johnston S, Seok Lee K, et al. Lancet Oncol. 2018;19(1):87-100.
7. Moynahan ME, Chen D, He W, et al. Br J Cancer. 2017;116(6):726-730002E
8. The Cancer Genome Atlas Network. Comprehensive molecular portraits of human breast tumours. Nature. 2012;490(7418):61-70.
9. Sobhani N, Roviello G, Corona SP et al. The prognostic value of PI3K mutational status in breast cancer: a meta-analysis. J Cell Biochem. 2018;119(6):4287-4292.

10. Sabine V, Crozier C, Brookes C, et al. Mutational analysis of PI3K/AKT signaling pathway in tamoxifen exemestane adjuvant multinational pathology study. Journal of Clinical Oncology. 2014;32:2951-2958.
11. Miller TW, Rexer BN, Garrett JT, et al. Mutations in the Phosphatidylinositol 3-Kinase Pathway: Role in Tumor Progression and Therapeutic Implications in Breast Cancer. Breast Cancer Res. 2011.
12. Saal LH, Johansson P, Holm K. Poor prognosis in carcinoma is associated with a gene expression signature of aberrant PTEN tumor suppressor pathway activity. PNAS. 2007;104(18):7564-7569.
13. Thomssen, C., et al. (2020, February 10). International Consensus Conference for Advanced Breast Cancer, Lisbon 2019: ABC5 Consensus – Assessment by a German Group of Experts. Retrieved June 16, 2020, from https://www.karger.com/Article/FullText/505957

# # #

Novartis Media Relations
E-mail: media.relations@novartis.com

Anja von Treskow
Novartis External Communications
+41 79 392 8697 (mobile)
anja.von_treskow@novartis.com

Julie Masow
Novartis Oncology Media Relations
+1 862 579 8456 (mobile)
julie.masow@novartis.com

Eric Althoff
Novartis US External Communications
+1 646 438 4335
eric.althoff@novartis.com

Novartis Investor Relations
Central investor relations line: +41 61 324 7944
E-mail: investor.relations@novartis.com

Central		North America	
Samir Shah	+41 61 324 7944	Sloan Simpson	+1 862 778 5052
Thomas Hungerbuehler	+41 61 324 8425		
Isabella Zinck	+41 61 324 7188		