Novartis International AG
Novartis Global Communications
CH-4002 Basel
Switzerland

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

MEDIA UPDATE

New Novartis data show Piqray® effectiveness across key biomarkers in patients with HR+/HER2- metastatic breast cancer

- *Biomarker analysis from Phase III SOLAR-1 study shows Piqray plus fulvestrant had clinical benefit regardless of presence of ESR1 mutations and genes implicated in CDK4/6i resistance*[1]

- *Piqray plus fulvestrant efficacy persists even with prior fulvestrant treatment; importance of targeting the PIK3CA driver mutation highlighted, as presented in a retrospective analysis of real-world evidence*[2]

- *Piqray is the only treatment specifically approved for HR+/HER2- mBC with a PIK3CA mutation, a key oncogenic driver of the disease*[3-5]

Basel, June 3, 2022 — Novartis today announced results of an exploratory retrospective biomarker analysis finding that different genetic mutation profiles in tumors harboring PIK3CA mutation did not affect treatment benefit with Piqray® (alpelisib) plus fulvestrant in patients with hormone receptor-positive, human epidermal growth factor receptor-2 negative (HR+/HER2-) advanced or metastatic breast cancer following progression on or after an endocrine-based regimen. Selected as an oral presentation at the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting (Abstract #1006), the retrospective analysis of data from the Phase III SOLAR-1 study found that the clinical benefit of the Piqray and fulvestrant combination was maintained regardless of genetic alterations in most biomarkers, including ESR1 and genes implicated in resistance to CDK4/6 inhibitors[1].

“This analysis evaluating alpelisib and fulvestrant across HR+/HER2- advanced breast cancer tumors with different genetic alterations confirms the importance of using alpelisib to selectively target PIK3CA as a major oncogenic driver in these tumors,” said Dejan Juric, MD, Director, Termeer Center for Target Therapies, Mass General Cancer Center in Boston.

“PIK3CA mutations affect approximately 40% of those with the HR+/HER2- subtype and are known oncogenic drivers of metastatic breast cancer, associated with endocrine resistance and an overall worse prognosis—so it’s critical for physicians to test and treat with Piqray for patients with PIK3CA mutations upfront consistent with ASCO and NCCN guidelines,” said Reshema Kemps-Polanco, Executive Vice President, US Oncology at Novartis.

Highlights from the SOLAR-1 biomarker retrospective analysis at ASCO

- Patients with ESR1 gene alterations achieved 12.0 months of median progression-free survival (mPFS) when treated with Piqray and fulvestrant compared to 6.5 months for those treated with fulvestrant alone[1].

- Even patients with FGFR1 and FGFR2 gene alterations, which have been associated with resistance to CDK4/6 inhibitors, had benefit when treated with Piqray plus fulvestrant (12.7 months and 9.6 months mPFS, respectively), compared to those treated with fulvestrant alone (3.8 months and 2.8 months mPFS, respectively)[1].

- The benefit seen with the Piqray and fulvestrant combination was independent of additional genetic alterations, including TP53, CCND1, MAP3K1 and ARID1A; genes in the MAPK pathway, genes implicated in CDK4/6 inhibitor resistance such as RB1[1].

Real-world evidence supports effectiveness of Piqray in tumors with PIK3CA mutation
A real-world retrospective analysis (Abstract #1055) showed clinical benefit for 157 patients with HR+/HER2- advanced or metastatic breast cancer with PIK3CA genetic mutation following treatment with Piqray plus fulvestrant, even when exposed to prior treatment with fulvestrant, confirming the oncogenic dependence of the tumor on the PIK3CA mutation[2]. In the analysis, prior fulvestrant treatment included CDK4/6 inhibior plus fulvestrant (74.5%), fulvestrant alone (33.8%), and non-CDK4/6 inhibitor plus fulvestrant (21.0%)[2].

About PIK3CA-mutated Breast Cancer
An estimated 361,826 people are diagnosed with metastatic breast cancer worldwide each year, and approximately 40% of those with HR+/HER2- subtype have tumors that harbor a PIK3CA mutation, which is associated with a poor prognosis[6-7].

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[3]. Piqray is approved in over 70 countries, including the US[6]. In the European member states, Piqray plus fulvestrant is approved after disease progression following endocrine therapy as monotherapy[8].

Novartis is continuing to reimagine cancer with additional trials of Piqray. To complement the SOLAR-1 study, EPIK-B5, a large Phase III clinical trial is conducted with Piqray in combination with fulvestrant following treatment with a CDK4/6 inhibitor and aromatase inhibitor[9]. Novartis is also studying the potential of Piqray in triple-negative breast cancer (TNBC) in the EPIK-B3 Phase III clinical trial, in advanced HER2+ breast cancer in the EPIK-B2 Phase III clinical trial and in ovarian cancer in the EPIK-O Phase III clinical trial[10-12].

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.

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

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,” “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 108,000 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. Juric D, Rugo HS, Reising A, et.al. Alpelisib (ALT) + fulvestrant (FUL) in patients (pts) with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) advanced breast cancer (ABC): Biomarker (BM) analyses by next-generation sequencing (NGS) from the SOLAR-1 study. 2022 American Society of Clinical Oncology (ASCO) Annual Meeting. Abstract #1006.
2. O'Shaughnessy J, Wöckel A, Pistilli B, et.al. Clincal outcomes with alpelisib (ALP) plus fulvestrant (FUL) after prior treatment (tx) with FUL in patients (pts) with advanced breast cancer (AMBC): a real-world (RW) analysis. 2022 American Society of Clinical Oncology (ASCO) Annual Meeting. Abstract #1055.
3. Piqray (alpelisib) Prescribing Information. East Hanover, New Jersey, USA: Novartis Pharmaceuticals Corporation.
4. The Cancer Genome Atlas Network. Comprehensive molecular portraits of human breast tumours. Nature. 2012;490(7418):61-70.
5. Mosele F, Stefanovska B, Lusque A, et al. Outcome and molecular landscape of patients with PIK3CA-mutated metastatic breast cancer. Ann Oncol. 2020;31(3):377-386.
6. Gheorghe D_BC Decision Resources_1-338_ 2017 (Digital Asset ID: 815601; Tag: 1004601/1235506).
7. Globocan 2020 (WHO), Cancer Today: Estimated number of new cases in 2020, worldwide, females, all ages_2020.
8. Novartis Data on File. Novartis Pharmaceuticals Corp: 2021.
9. Novartis Pharmaceuticals. Study to Assess the Efficacy and Safety of Alpelisib Plus Fulvestrant in Participants With HR-postitive (HR+), HER2-negative, Advanced Breast Cancer After Treatment With a CDK4/6 Inhibitor and an Aromatase Inhibitor: EPIK-B5 (October 27, 2021- November 27, 2026). Identifier: NCT05038735. https://www.clinicaltrials.gov/ct2/show/NCT05038735.
10. Novartis Pharmaceuticals. Study Assessing the Efficacy and Safety of Alpelisib + Nab-paclitaxel in Subjects With Advanced TNBC Who Carry Either a PIK3CA Mutation or Have PTEN Loss: EPIK-B3 (June 8, 2020-January 9, 2026). Identifier: NCT04251533. https://www.clinicaltrials.gov/ct2/show/NCT04251533.
11. Novartis Pharmaceuticals. EPIK-B2: A Two Part, Phase III, Multicenter, Randomized (1:1), Double-blind, Placebo-controlled Study to Assess the Efficacy and Safety of Alpelisib (BYL719) in Combination With Trastuzumab and

Pertuzumab as Maintenance Therapy in Patients With HER2-positive Advanced Breast Cancer With a PIK3CA Mutation. Identifier: NCT04208178. https://www.clinicaltrials.gov/ct2/show/ NCT04208178.
12. Novartis Pharmaceuticals. Alpelisib Plus Olaparib in Platinum-resistant/Refractory, High-grade Serous Ovarian Cancer, With no Germline BRCA Mutation Detected: EPIK-O (July 2, 2021-January 31, 2025). Identifier: NCT04729387. https://www.clinicaltrials.gov/ct2/show/NCT04729387.

# # #

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

Ashley Buford
Novartis Oncology Communications
+1 201 953 4364
ashley.buford@novartis.com

Julie Masow
Novartis US External Communications
+1 862 579 8456
julie.masow@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	+1 862 345 4440
Nicole Zinsli-Somm	+41 61 324 3809	Alina Levchuk	+1 862 778 3372
Isabella Zinck	+41 61 324 7188	Parag Mahanti	+1 973 876 4912