Novartis International AG
Novartis Global Communications
CH-4002 Basel
Switzerland

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MEDIA & INVESTOR RELEASE

Novartis data highlight efficacy of Piqray® in HR+/HER2- metastatic breast cancer with a PIK3CA driver mutation immediately post-CDK4/6i

- *New data underscore efficacy of Piqray, even in those patients with a short treatment duration on prior CDK4/6i or with ESR1 mutations, biomarkers of endocrine resistance*[1-5]

- *Recent guideline updates support use of Piqray with fulvestrant for postmenopausal HR+/HER2- PIK3CA-mutated mBC patients immediately after failure on prior CDK4/6i treatment*[6]

- *Piqray works synergistically with fulvestrant across the PI3K and estrogen receptor pathways, respectively—remaining the only treatment specifically approved for mBC with a PIK3CA mutation, a known oncogenic driver of the disease*[7-9]

- *Five BYLieve presentations include data on longer-term follow-up and ESR1 mutations, which occur in up to 56% of patients with HR+/HER2- mBC*[1-5,10-11]

Basel, December 10, 2021 — Novartis today announced new Piqray® (alpelisib) data indicating benefit across a broad range of patient and disease characteristics as seen in analyses from all three cohorts of BYLieve. BYLieve is an ongoing Phase II, open-label, 3-cohort non-comparative study evaluating Piqray with endocrine therapy including men and pre- and postmenopausal women with hormone-receptor positive, human epidermal growth factor receptor-2 negative (HR+/HER2-) advanced or metastatic breast cancer (mBC) who have progressed on or after prior therapies, including CDK4/6 inhibitor plus endocrine therapy[1-5]. These data will be presented at the 2021 San Antonio Breast Cancer Symposium (SABCS) from December 7-10.

“The data from all three cohorts of the BYLieve study have value for the medical community and for the patients we care for with mBC, because these cohorts show a benefit from alpelisib in the post-CDK4/6i setting for patients with HR+/HER2- PIK3CA-mutated cancer,” said Dr. Hope S. Rugo, Director, Breast Oncology and Clinical Trials Education, University of California San Francisco (UCSF) Helen Diller Family Comprehensive Cancer Center. “Beyond illustrating the efficacy and safety of alpelisib, regardless of the duration of prior CDK4/6i treatment, the data provide meaningful insights into how alpelisib may benefit different subgroups of patients.”

Highlights from the BYLieve data presented at SABCS

- **BYLieve Cohort A** (P1-18-03)**:** Updated safety and efficacy data after 18 months of follow-up showed median overall survival improvement of 26.4 months (95% CI: 21.0-30.5) for patients treated with Piqray plus fulvestrant immediately following CDK4/6i plus an AI[1]. The most common all-grade adverse events (AEs) (n=127) were diarrhea (63.8%), hyperglycemia (59.8%), nausea (46.5%) and rash (31.5%)[1].

- **BYLieve Cohort C** (PD13-05)**:** The third and final BYLieve cohort included patients who received chemotherapy or endocrine therapy as immediate prior treatment, who could have received prior CDK4/6i as well[2].
    - The primary endpoint was met with 48.7% (95% CI: 39.3%-58.2%) of patients alive and without disease progression at six months[2].
    - Data confirm clinically relevant activity of Piqray as a targeted therapy for PIK3CA as a driver oncogene[2].
    - No new safety signals were observed, with the most common all-grade AEs (n=126) being hyperglycemia (65.1%), diarrhea (52.4%), nausea (40.5%) and rash (38.9%)[2].

- **BYLieve Cohorts A & B** (P1-18-08; P5-13-03; PD15-01)**:** Exploratory biomarker and post-hoc analyses demonstrated efficacy with Piqray plus fulvestrant/letrozole in CDK4/6i-resistant mBC, as seen in patients with early discontinuation of the prior CDK4/6i (Cohort A: ≤6 months median PFS of 12.0 months and >6 months median PFS of 6.2 months; HR=0.51; 95% CI: 0.29-0.89; Cohort B: ≤6 months median PFS of 5.9 months and >6 months median PFS of 5.6 months; HR=0.72; 95% CI: 0.45-1.18), supporting the use of Piqray plus endocrine therapy as an immediate next-line option in these patients[3]. Grade ≥3 AEs were experienced by 84.6% (n=22) and 66.0% (n=66) of patients in the ≤6 months and >6 months subgroups, respectively, in Cohort A and by 62.5% (n=20) and 72.5% (n=66) of patients in the ≤6 months and >6 months subgroups, respectively, in Cohort B[3].

Additionally, the exploratory ctDNA analysis from Cohorts A and B (median PFS of 7.3 months and 5.7 months in Cohorts A and Cohort B, respectively) found that Piqray was effective in the post-CDK4/6i setting regardless of endocrine therapy partner and tumor genomic profile and other mutations associated with CDK4/6i resistance[4]. Across the three cohorts no new safety signals were observed, even with longer exposure, as seen in Cohort A, confirming no cumulative toxicities with Piqray[1-3].

An estimated 361,826 people are diagnosed with mBC worldwide each year, and approximately 40% of those with HR+/HER2- subtype have a PIK3CA mutation, which is associated with a poor prognosis[8-9].

Visit https://www.hcp.novartis.com/virtual-congress/sabcs-2021/ for the latest information from Novartis, including our commitment to the Oncology community, and access to our SABCS Virtual Scientific Program data presentations (for registered participants).

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[7]. Piqray is approved in 64 countries, including the US and European member states[12].

Novartis is continuing to reimagine cancer with additional trials of Piqray. EPIK-B5 will be a large Phase III clinical trial of Piqray in combination with fulvestrant to complement the SOLAR-1 study[13]. 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[14-16].

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.

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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 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 press release 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 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 108,000 people of more than 140 nationalities work at Novartis around the world. Find out more at https://www.novartis.com.

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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
Thomas Hungerbuehler	+41 61 324 8425	Alina Levchuk	+1 862 778 3372
Isabella Zinck	+41 61 324 7188	Parag Mahanti	+1 973 876 4912