



# Pfizer Presents Final Phase 2 Data on Investigational PARP Inhibitor Talazoparib in Patients with Germline BRCA-Positive Advanced Breast Cancer

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Phase 3 EMBRACA trial of talazoparib in advanced gBRCA+ breast cancer now fully enrolled

**“Every day, I see the devastating effects of gBRCA+ advanced breast cancer - one of the most common forms of inherited breast cancer.”**

Pfizer Inc. (NYSE:PFE) today announced Phase 2 data showing that its investigational, dual-mechanism poly ADP ribose polymerase (PARP) inhibitor, talazoparib, demonstrated anti-tumor activity in patients with germline (inherited) BRCA1/2-positive (gBRCA+) advanced breast cancer. Results from the Phase 2 ABRAZO trial were presented during an oral session at the 53rd Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago.

“Every day, I see the devastating effects of gBRCA+ advanced breast cancer – one of the most common forms of inherited breast cancer,” said Nicholas C. Turner, MD, PhD, consultant medical oncologist at the Royal Marsden Hospital in London, United Kingdom. “As we learn more about the genetic drivers of cancer, mechanisms such as PARP inhibition are emerging as a potential therapeutic approach for this patient population.”

ABRAZO is an open-label Phase 2, 2-stage, single arm, parallel cohort study that investigated the clinical efficacy and safety of single-agent talazoparib in 83 evaluable, heavily pretreated gBRCA+ advanced breast cancer patients. The primary endpoint was objective response rate (ORR) by independent radiology review.

Cohort 1 consisted of 49 patients who previously responded to platinum-based chemotherapy and subsequently developed disease progression. A 21% ORR (95% CI: 10-35) was observed in this group of patients. Cohort 2 consisted of 35 patients who developed disease progression following at least three lines of non-platinum-based therapy. This group of patients had a 37% ORR (95% CI: 22-55).

The most common adverse events (AEs) observed in at least 20% of patients consisted of anemia (51.8%), thrombocytopenia (32.5%), neutropenia (26.5%), fatigue (44.6%), nausea (42.2%), diarrhea (32.5%), decreased appetite (24.1%), dyspnea (24.1%), alopecia (21.7%), back pain (21.7%) and vomiting (20.5%). Grade 3 or 4 AEs observed in at least 10% of patients were anemia (34.9%), thrombocytopenia (19.3%) and neutropenia (14.5%). Hematological AEs were addressed with dose management. No clinically significant cardiovascular events were observed. Discontinuation rates due to drug-related AEs were low (4%).

“The activity observed in patients with gBRCA+ advanced breast cancer in the ABRAZO trial is highly encouraging. The Phase 3 EMBRACA trial was designed to build upon these results to determine whether talazoparib represents a potential treatment option in this type of breast cancer,” said Mace Rothenberg, MD, chief development officer, Oncology, Pfizer Global Product Development.

Talazoparib is also being assessed in the open-label Phase 3 randomized, parallel, 2-arm EMBRACA trial. EMBRACA is evaluating talazoparib vs. protocol-specific physician’s choice of chemotherapy in patients with advanced and/or metastatic gBRCA+ breast cancer who have received zero to three prior chemotherapy regimens for advanced disease. The EMBRACA trial has completed enrollment and results will be made available at a future date.

### **About the ABRAZO Trial**

Patients enrolled in the multicenter, open-label Phase 2, 2-stage, parallel cohort study received talazoparib once daily for 21 days in repeated 21-day cycles. Patients had triple negative breast cancer, hormone receptor-positive (HR+) breast cancer, or human epidermal growth factor 2 (HER2)-positive breast cancer that was refractory to HER2-targeted therapy. The median number of prior lines of chemotherapy for advanced breast

cancer was two in Cohort 1 and four in Cohort 2. Investigators required at least five objective responses per cohort in  $\leq 35$  patients to progress from the first stage of the trial to the second stage. Both cohorts met the response criteria for advancement.

### **About Talazoparib**

Talazoparib is an investigational anticancer compound called a PARP (poly ADP ribose polymerase) inhibitor, which is being evaluated in gBRCA+ breast cancer, as well as other cancer types with deficiencies in DNA damage repair (DDR). Preclinical studies suggest that talazoparib has a dual mechanism of action, with the potential to induce tumor cell death by blocking PARP enzyme activity and trapping PARP on the sites of DNA damage. Talazoparib has not been approved by any regulatory authorities for the treatment of any disease.

### **About Germline BRCA1/2-Positive Breast Cancer**

BRCA1 and BRCA2 are human genes that produce proteins involved in DNA repair. When either of these genes is altered or mutated, DNA repair may not progress correctly. This can lead to the development of certain types of cancer - such as breast cancer.<sup>1,2,3</sup> BRCA mutations can be hereditary (germline) or occur spontaneously (sporadic).<sup>1</sup> BRCA mutations are the most common cause of hereditary breast cancers, and up to 65% of women who inherit a BRCA mutation will develop breast cancer by age 70.<sup>1,4</sup> Epidemiologic studies indicate that individuals with gBRCA+ status are diagnosed with breast cancer at a median age of 40-45, which is approximately 20 years younger than the overall breast cancer population.<sup>5</sup> Literature indicates that 5-10% of all breast cancer patients have a gBRCA mutation.<sup>6</sup>

### **About Pfizer Oncology**

Pfizer Oncology is committed to pursuing innovative treatments that have a meaningful impact on those living with cancer. As a leader in oncology speeding cures and accessible breakthrough medicines to patients, Pfizer Oncology is helping to redefine life with cancer. Our strong pipeline of biologics, small molecules and immunotherapies, one of the most robust in the industry, is studied with precise focus on identifying and translating the best scientific breakthroughs into clinical application for patients across a wide range of cancers. By working collaboratively with academic institutions, individual researchers, cooperative research groups, governments and licensing partners, Pfizer Oncology strives to cure or control cancer with its breakthrough medicines. Because Pfizer Oncology knows that success in oncology is not measured solely by the medicines you manufacture, but rather by the meaningful partnerships you make to have a more

positive impact on people's lives.

## **Working together for a healthier world®**

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer health care products. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at [www.pfizer.com](http://www.pfizer.com). In addition, to learn more, please visit us on [www.pfizer.com](http://www.pfizer.com) and follow us on Twitter at @Pfizer and @Pfizer\_News, LinkedIn, YouTube and like us on Facebook at [Facebook.com/Pfizer](https://www.facebook.com/Pfizer).

**DISCLOSURE NOTICE:** The information contained in this release is as of June 3, 2017. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about a product candidate, talazoparib, including its potential benefits, that involve substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, the uncertainties inherent in research and development, including, without limitation, the ability to meet anticipated clinical trial commencement and completion dates and regulatory submission dates, as well as the possibility of unfavorable clinical trial results, including unfavorable new clinical data and additional analyses of existing clinical data; whether and when new drug applications may be filed in any jurisdictions for talazoparib; whether and when such applications may be approved by regulatory authorities, which will depend on the assessment by such regulatory authorities of the benefit-risk profile suggested by the totality of the efficacy and safety information submitted; decisions by regulatory authorities regarding labeling and other matters that could affect the availability or commercial potential of talazoparib; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2016 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at [www.sec.gov](http://www.sec.gov) and [www.pfizer.com](http://www.pfizer.com).

1 National Cancer Institute. BRCA1 and BRCA2: Cancer Risk and Genetic Testing. <https://www.cancer.gov/about-cancer/causes-prevention/genetics/brca-fact-sheet>. Accessed June 1, 2017. 2 Evers et al. A high throughput pharmaceutical screen identifies compounds with specific toxicity against BRCA2-deficient tumors. *Clin Cancer Res*. 2010 Jan 1; 16(1): 99-108. 3 Livraghi L, Garber J. PARP inhibitors in the management of breast cancer: Current data and future prospects. *BMC Medicine*. 2015;13:188. 4 American Cancer Society. Breast Cancer Risk Factors You Cannot Change. <https://www.cancer.org/cancer/breast-cancer/risk-and-prevention/breast-cancer-risk-factors-you-cannot-change.html>. Accessed June 1, 2017. 5 Kim R. et al. Incidence of Germline BRCA1- and BRCA2-Mutated Breast Cancer in the United States. *San Antonio Breast Cancer Symposium*. 2016. 6 Peshkin BN, Alabek ML, Issacs C. BRCA 1/ 2 mutations and triple negative breast cancers. *Breast Dis*. 2010; 32(1-2):25-33.

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