TESARO Announces European Commission Approval of ZEJULA® for Women With Recurrent Ovarian Cancer

November 20, 2017

- ZEJULA is the first PARP inhibitor approved in Europe for women with recurrent ovarian cancer, regardless of *BRCA* mutation or biomarker status
- Approval supported by robust data from a randomized, well-controlled Phase 3 trial
- Only PARPi to offer once-daily, oral dosing to enable convenient administration for maintenance treatment
- First commercial launches planned for Germany and the UK this December

ZUG, Switzerland, Nov. 20, 2017 (GLOBE NEWSWIRE) -- TESARO, Inc. (NASDAQ:TSRO), an oncology focused biopharmaceutical company, announced today that the European Commission (EC) has granted marketing authorization for ZEJULA® (niraparib) as a monotherapy for the maintenance treatment of adult patients with platinum-sensitive relapsed high grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete response (CR) or partial response (PR) to platinum-based chemotherapy. ZEJULA is the first once-daily, oral poly (ADP-ribose) polymerase (PARP)1/2 inhibitor to be approved in Europe that does not require *BRCA* mutation or other biomarker testing.

A PDF accompanying this announcement is available at
http://www.globenewswire.com/NewsRoom/AttachmentNg/0697ad84-510c-4ee8-8c22-0573cc9636ba

“We want to express our gratitude to all of the women who selflessly participated in the ZEJULA clinical development program. I would also like to thank our partners at ENGOT for their diligence in conducting the ENGOT-OV16/NOVA trial, which was carried out with the highest level of scientific rigor. The unique design of this trial, which included women both with and without germline *BRCA* mutations, allowed us to independently determine that ZEJULA provides significant progression-free survival improvement in a very broad patient population,” said Mary Lynne Hedley, Ph.D., President and Chief Operating Officer of TESARO. “The EC approval of ZEJULA marks TESARO’s second product approval in Europe this year. We are committed to working with healthcare providers, payers and patient groups to enable access to this paradigm-changing treatment as quickly as possible.”

ZEJULA was approved by the U.S. Food and Drug Administration on March 27, 2017 and is marketed by TESARO in the United States, where it is currently the most frequently prescribed PARP inhibitor for patients with ovarian cancer. TESARO plans to launch ZEJULA in Germany and the UK this December, with launches in additional European countries to follow beginning in 2018, based on local reimbursement and availability timelines. Germany and the UK are two of the 17 countries where TESARO currently has a direct presence in Europe.

“Today’s approval of ZEJULA is an exciting step forward for the ovarian cancer community in Europe. While platinum-based chemotherapy has proven to be effective, its efficacy unfortunately diminishes over time, and progression-free survival becomes shorter after each successive platinum treatment,” said Mansoor Raza Mirza, M.D., ENGOT-OV16/NOVA Study Chair and Chief Oncologist at Rigshospitalet, Copenhagen. “ZEJULA now provides an opportunity to increase progression-free survival after platinum therapy, and will have a profound impact for women and their families.”

The EC approval of ZEJULA was based on data from the clinically rigorous ENGOT-OV16/NOVA trial, a double-blind, placebo-controlled, international Phase 3 study of ZEJULA that enrolled 553 patients with recurrent ovarian cancer who had achieved either a PR or CR to their most recent platinum-based chemotherapy. The primary endpoint of the trial was progression free survival (PFS). Approximately two-thirds of study participants did not have germline *BRCA* mutations. Progression in the NOVA study was determined by a robust, unbiased, blinded central review to be the earlier of radiographic or clinical progression. ZEJULA significantly increased PFS in patients with or without germline *BRCA* mutations as compared to the control arm. Treatment with ZEJULA reduced the risk of disease progression or death by 73% in patients with germline *BRCA* mutations (hazard ration (HR) 0.27) and by 55% in patients without germline *BRCA* mutations (HR 0.45). The magnitude of benefit was similar for patients entering the trial with a PR or a CR.

“With the introduction of ZEJULA, treatment of women with recurrent ovarian cancer will improve markedly,” said Professor Dr. Andreas Du Bois, Center Director of Gynecology & Gynecologic Oncology, Kliniken Essen-Mitte (Germany) and Co-Founder and Past Chair of the European Network of Gynecological Oncological Trial Groups (ENGOT). “Patients and their physicians are now empowered with an additional option to utilize after a response to chemotherapy, regardless of *BRCA* mutation status, where the previous alternative for most was a period of watching and waiting instead of actively controlling their disease.”

The approved starting dose of ZEJULA is 300 milligrams once per day. According to the European summary of product characteristics (SmPC), in patients below 58 kilograms, a starting dose of 200 milligrams once per day may be considered. The most commonly administered dose of ZEJULA over the course of the Phase 3 NOVA clinical trial was 200 milligrams once per day, following dose modification. Further exploratory analyses of the NOVA study indicated that individual dose modification maintained efficacy and reduced the rate of new adverse events[1].

The most common grade 3/4 adverse reactions to ZEJULA included thrombocytopenia (34%), anemia (25%), neutropenia (20%), and hypertension (8%). Following dose adjustment based on individual tolerability, the incidence of grade 3/4 thrombocytopenia was low, approximately 1% after month three. The majority of hematologic adverse events were successfully managed via dose modification, and discontinuation of therapy due to thrombocytopenia, neutropenia and anemia occurred in 3%, 2% and 1% of patients, respectively.

“We welcome the decision by the EC to approve ZEJULA for women with recurrent ovarian cancer,” said Elisabeth Baugh, Chair of the World Ovarian Cancer Coalition. “This decision will have a real and meaningful impact on women's lives, providing them a new treatment option and greater choice. Globally, we are lacking effective treatments for ovarian cancer, so this is a much-needed addition.”

About the ZEJULA® (niraparib) ENGOT-OV16/NOVA Clinical Trial
ENGOT-OV16/NOVA was a double-blind, placebo-controlled, international Phase 3 trial of niraparib that enrolled 553 patients with recurrent ovarian cancer who were in a response to their most recent platinum-based chemotherapy. Patients were enrolled into one of two independent cohorts based on germline *BRCA* mutation status. One cohort enrolled patients who were germline *BRCA* mutation carriers (g*BRCA*mut), and the second cohort enrolled patients who were not germline *BRCA* mutation carriers (non-g*BRCA*mut) and included patients with HRD-positive and HRD-negative tumors. Within each cohort, patients were randomized 2:1 to receive niraparib or placebo and were treated continuously with placebo or 300 milligrams of niraparib, dosed as three 100 milligram tablets once per day, until progression. The primary endpoint of this study was progression-free survival (PFS). Secondary endpoints included patient-reported outcomes,

chemotherapy-free interval length, PFS 2, overall survival, and other measures of safety and tolerability. More information about this trial is available at http://clinicaltrials.gov/show/NCT01847274.

Among patients who were germline *BRCA* mutation carriers, the niraparib arm successfully achieved statistical significance over the control arm for the primary endpoint of PFS, with a HR of 0.26 (95% CI, 0.173-0.410). The median PFS for patients treated with niraparib was 21.0 months, compared to 5.5 months for control (*p<0.0001*). Niraparib also showed statistical significance for patients in the non-germline *BRCA* mutation cohort. The niraparib arm successfully achieved statistical significance over the control arm for the primary endpoint of PFS, with a HR of 0.45 (95% CI, 0.338-0.607). The median PFS for patients treated with niraparib was 9.3 months, compared to 3.9 months for control (*p<0.0001*). Secondary endpoint analyses, including chemotherapy-free interval, time to first subsequent treatment, and PFS 2 were all statistically significant and favored niraparib over control for patients in both the g*BRCA*mut and non-g*BRCA*mut cohorts. Patient-reported outcome results from validated survey tools indicated that niraparib-treated patients reported no difference from control in measures associated with quality of life.

The full results of the ENGOT-OV16/NOVA trial were presented in detail at the European Society for Medical Oncology (ESMO) 2016 Congress in Copenhagen on October 8, 2016 by Dr. Mansoor Raza Mirza, M.D., Medical Director of the Nordic Society of Gynecologic Oncology (NSGO) and Principal Investigator. These data were simultaneously published in the *New England Journal of Medicine*.

Select Important Safety Information
Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML) was reported in patients treated with ZEJULA. Discontinue ZEJULA if MDS/AML is confirmed.

Hematologic adverse reactions (thrombocytopenia, anemia and neutropenia) have been reported in patients treated with ZEJULA. Monitor complete blood counts (CBCs) weekly for the first month of treatment and modify the dose as needed. After the first month, it is recommended to monitor CBCs for the next 10 months of treatment, and periodically after this time. Based on individual laboratory values, weekly monitoring for the second month may be warranted.

Hypertension and hypertensive crisis have been reported in patients treated with ZEJULA. Pre-existing hypertension should be adequately controlled before starting ZEJULA. Monitor blood pressure monthly for the first year and periodically thereafter during treatment with ZEJULA. ZEJULA should be discontinued in case of hypertensive crisis or if medically significant hypertension cannot be adequately controlled with antihypertensive therapy.

Based on its mechanism of action, ZEJULA can cause fetal harm. Advise females of reproductive potential of the possible risk to a fetus and to use effective contraception during treatment and for six months after receiving the final dose. Because of the potential for serious adverse reactions in breastfed infants from ZEJULA, advise a lactating woman not to breastfeed during treatment with ZEJULA and for one month after receiving the final dose.

In clinical studies, the most common adverse reactions included: thrombocytopenia, anemia, neutropenia, nausea, constipation, vomiting, abdominal pain, diarrhea, dyspepsia, urinary tract infection, fatigue/asthenia, decreased appetite, headache, dizziness, dysgeusia, palpitations, insomnia, nasopharyngitis, dyspnea, cough, and hypertension.

Additional Clinical Trials of Niraparib
TESARO is building a robust niraparib franchise by assessing activity across multiple tumor types and by evaluating several potential combinations of niraparib with other therapeutics. The ongoing development program for niraparib includes a Phase 3 trial in patients who have received first-line treatment for ovarian cancer (the PRIMA trial) and a registrational Phase 2 trial in patients who have received multiple lines of treatment for ovarian cancer (the QUADRA trial). Several combination studies are also underway, including trials of niraparib plus pembrolizumab (the TOPACIO trial) and niraparib plus bevacizumab (the AVANOVA trial).

Additional trials of niraparib in ovarian, breast and lung cancers are planned. The studies will assess the effect of niraparib alone and in combination with other therapies in a variety of treatment settings.

Janssen Biotech has licensed rights to develop and commercialize niraparib specifically for patients with prostate cancer worldwide, except in Japan.

About Ovarian Cancer in Europe
Europe has one of the highest incidences of ovarian cancer in the world with approximately 45,000 women diagnosed each year[2,][3]. Ovarian cancer affects approximately 1.3 in 10,000 people in the European Union, where it is the sixth-most common cancer and the fifth-most frequent cause of cancer death among women2.[4]. Despite high initial response rates to platinum-based chemotherapy, approximately 85% of women with advanced ovarian cancer will experience a recurrence of the disease after first-line treatment[5]. The efficacy of chemotherapy also diminishes over time.

About ZEJULA (niraparib)
ZEJULA is a once-daily, oral poly (ADP-ribose) polymerase (PARP) 1/2 inhibitor that is indicated in the European Union as a monotherapy for the maintenance treatment of adult patients with platinum-sensitive relapsed high grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy. In preclinical studies, ZEJULA concentrates in the tumor relative to plasma, delivering greater than 90% durable inhibition of PARP 1/2 and a persistent antitumor effect.

About TESARO
TESARO is an oncology-focused biopharmaceutical company devoted to providing transformative therapies to people bravely facing cancer. For more information, visit www.tesarobio.com and follow us on Twitter and LinkedIn.

Forward Looking Statements
To the extent that statements contained in this press release are not descriptions of historical facts regarding TESARO, they are forward-looking statements reflecting the current beliefs and expectations of management made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Words such as "may," "will," "expect," "anticipate," "estimate," "intend," and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements. Forward-looking statements in this release involve substantial risks and uncertainties that could cause our commercial launch efforts, clinical development programs, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, risks associated with timing for successful ZEJULA commercial launch in specific European countries, competition, risks related to pricing and reimbursement, risks related to manufacturing and supply, risks related to intellectual property, and other risks and uncertainties that could affect the availability or commercial potential of ZEJULA *in Europe. TESARO undertakes no obligation to update or revise any forward-looking statements. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to the business of the Company in general, see TESARO's Annual Report on Form 10-K for the year ended December 31, 2016 and Quarterly Report on Form 10-Q for the quarter ended September 30, 2017.*

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[1] Wang J et al. The Exposure-Response Relationship of Niraparib in Patients with g*BRCA*mut and Non-g*BRCA*mut: Results from the ENGOT-OV16/NOVA Trial. ESMO; 2017 Sep 8-12; Madrid, Spain.
[2]World Cancer Research Fund International. http://www.wcrf.org/int/cancer-facts-figures/data-specific-cancers/ovarian-cancer-statistics (Last accessed 18 November 2017)
[3] EUCAN http://eco.iarc.fr/eucan/Country.aspx?ISOCountryCd=930 (Last accessed 18 November 2017)
[4] ENGAGe, Ovarian Cancer Fact Sheet. https://engage.esgo.org/media/2017/08/ENGAGe_What_is_ovarian_cancer_en_V01.pdf (Last accessed 18 November 2017)
[5] Lorusso, D., Mancini, M., Di Rocco, R., Fontanelli, R., & Raspagliesi, F. (2012). The role of secondary surgery in recurrent ovarian cancer. International Journal of Surgical Oncology

Source: TESARO, Inc.