Data From TOPACIO Trial Reported at SGO Demonstrates Compelling Clinical Activity of ZEJULA in Combination With an Anti-PD-1 Antibody in Patients With Platinum Resistant/Refractory Ovarian Cancer

March 26, 2018

- **Efficacy of niraparib in combination with an anti-PD-1 mAb surpasses historical efficacy benchmarks for PD-1 or PARP monotherapies in difficult-to-treat types of ovarian cancer, regardless of biomarker status**
- **Potential approach to reduce incidence of Grade 3 or 4 thrombocytopenia identified based on retrospective analysis of data from Phase 3 NOVA trial**

NEW ORLEANS, March 26, 2018 (GLOBE NEWSWIRE) -- TESARO, Inc. (NASDAQ:TSRO), an oncology-focused biopharmaceutical company announced the presentation of maturing data from the TOPACIO trial of niraparib in combination with an anti-PD-1 monoclonal antibody, KEYTRUDA® during a plenary session today at the 2018 Society for Gynecologic Oncology (SGO) Annual Meeting on Women's Cancer in New Orleans, Louisiana. In addition, retrospective data analyses of the Phase 3 ENGOT-OV16/NOVA study that could potentially reduce Grade 3/4 thrombocytopenia in niraparib treated patients was presented in the plenary session on Sunday, March 25.

"Patients with platinum-resistant or platinum-refractory ovarian cancer have limited treatment options available to them. Approximately 10,000 women in each of the US and EU begin treatment for platinum-resistant or refractory ovarian cancer each year," said Mary Lynne Hedley, Ph.D., President and COO of TESARO. "Preliminary results from TOPACIO suggest the combination of niraparib and an anti-PD-1 antibody could provide meaningful clinical benefit to these patients, regardless of biomarker status. Planning of a registration study is underway to support approval of ZEJULA and TSR-042 combination therapy for these patients. TSR-042 is TESARO's anti-PD-1 antibody, which is currently in a registration study for MSI-H tumors."

"These data provide a compelling initial step in our ovarian cancer development strategy which is progressing from monotherapy ZEJULA utilized in PRIMA, NOVA and QUADRA to doublet and triplet combination approaches with anti-PD-1 antibodies and bevacizumab," said Marty Huber, M.D., Senior Vice President and Chief Medical Officer of TESARO. "Our ultimate goal is to maximize the benefit to women across the full spectrum of ovarian cancer"

Phase 2 TOPACIO Data Demonstrate Activity in Platinum-Resistant and Platinum-Refractory Ovarian Cancer Patients, Regardless of Biomarker Status
TOPACIO is a Phase 1/2 clinical trial designed to evaluate the safety and efficacy of niraparib plus KEYTRUDA® (pembrolizumab) in patients with recurrent, platinum-resistant ovarian cancer or triple negative breast cancer. Niraparib administered orally, once-daily, at a dose of 200 milligrams is being evaluated in combination with 200 milligrams of pembrolizumab administered intravenously on day one of each 21-day treatment cycle in two patient cohorts; platinum-resistant/refractory ovarian cancer and triple-negative breast cancer. Endpoints include RECIST response rate, duration of response, disease control rate, progression-free survival and overall survival. Data presented at SGO were from the group of patients with ovarian cancer.

At the time of data cutoff, of the 62 patients enrolled, 60 were evaluable; 45% had been treated with 3 or more prior lines of chemotherapy, 97% with prior taxane, 63% received prior bevacizumab, and 29% were platinum refractory. The majority (73%) did not have a *BRCA* mutation. Data indicate an overall response rate (ORR; including CR and PR) of 25% and a disease control rate (DCR; CR+PR+SD) of 68%; ORR was 24% in the platinum refractory population. Response rates were not dependent on biomarker status; ORR was 26% (9/34) in patients without a tumor *BRCA* mutation (t*BRCA*wt), and 29% (7/24) in patients with HRD-negative tumors. Duration of response was immature, with 9 of 15 (60%) of responders remaining on treatment, and over one-half of patients with disease control continuing on treatment or having already received treatment for over 6 months.

For patients with platinum-resistant ovarian cancer, response to chemotherapy is 5-18%, including the most commonly prescribed regimen in the U.S., bevacizumab plus pegylated liposomal doxorubicin[1]. Platinum refractory patients typically have even lower response rates and NCCN treatment guidelines recommend clinical trials for these patients[2]. Historical response to PARP inhibitors is 5-10% in patients without *BRCA* mutations who have platinum resistant disease[3] and 0-14% in those with *BRCA* mutations and platinum refractory disease[4]. Response rates of 10-15% have been reported with anti-PD-1 antibodies in this ovarian cancer population[5].

The combination of niraparib with pembrolizumab was well tolerated with an incidence of Grade 3/4 thrombocytopenia of 9%. In addition to thrombocytopenia, the other most commonly observed Grade ?3 adverse events included anemia (19%) and neutropenia (6%).

Abstracts containing additional data from the TOPACIO trial, including results from patients with platinum-resistant ovarian cancer and patients with triple-negative breast cancer, have been submitted to the American Society for Clinical Oncology (ASCO) Annual Meeting. The TOPACIO trial is being conducted in collaboration with Merck Sharp & Dohme B.V., a subsidiary of Merck & Co., Inc., which is providing support for the trial.

A Retrospective Analysis of Phase 3 ENGOT-OV16/NOVA Trial Identified Predictors of Early Dose Modification for Niraparib
A retrospective analysis of the Phase 3 NOVA trial identified two baseline characteristics, patient body weight less than 170 pounds (77 kilograms) or platelet count of <150,000/µL to be significant factors for Grade 3 or 4 thrombocytopenia. The incidence of thrombocytopenia in the first month in this population was 35% in the NOVA study vs 12% in those with higher weight and platelet counts. By month 4, of the patients who remained on treatment, 83% with body weight < 170lbs or platelet count of <150,000/µL at baseline were receiving a dose of niraparib <300 milligrams. With dose interruptions, this group's average daily dose was 207 milligrams in the first two months of niraparib therapy in NOVA. Regardless, efficacy was uncompromised (HR: 1.01 (95%CI: 0.69, 1.48)) in patients receiving a 200 milligram versus 300 milligram dose of niraparib. Of note, in TOPACIO, where starting dose is 200 milligrams, a 9% incidence of Grade 3 or 4 thrombocytopenia was reported.

"This analysis provides physicians with new information to help quickly identify the most appropriate dose for each of their patients," said Dr. Mansoor Raza Mirza, M.D., Medical Director of the Nordic Society of Gynecologic Oncology (NSGO) and principal investigator on the ENGOT-OV16/NOVA trial. "This information is particularly important as we move towards combination treatment approaches with niraparib, which are currently being studied in multiple ongoing clinical trials."

About ZEJULA® (Niraparib)
Niraparib is marketed in the United States and Europe under trade name ZEJULA®. ZEJULA (niraparib) is a poly(ADP-ribose) polymerase (PARP) inhibitor indicated for the maintenance treatment of adult patients with recurrent 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.

ZEJULA (niraparib) Select Important Safety Information
Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML) was reported in patients treated with ZEJULA in some clinical studies. Discontinue ZEJULA if MDS/AML is confirmed. Hematologic adverse reactions (thrombocytopenia, anemia and neutropenia) have been reported in patients treated with ZEJULA. Do not start ZEJULA until patients have recovered from hematological toxicity caused by previous chemotherapy (? Grade 1). Monitor complete blood counts weekly for the first month, monthly for the next 11 months of treatment, and periodically after this time.

Hypertension and hypertensive crisis have been reported in patients treated with ZEJULA. Monitor blood pressure and heart rate monthly for the first year and periodically thereafter during treatment with ZEJULA. Closely monitor patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension.

Based on its mechanism of action, ZEJULA can cause fetal harm. Advise females of reproductive potential of the potential 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.

About TSR-042

TSR-042 is a monoclonal antibody targeting PD-1 and was developed as part of the collaboration between TESARO and AnaptysBio, Inc. This collaboration was initiated in March of 2014, and is focused on the development of monospecific antibody drugs targeting PD-1, TIM-3 (TSR-022), and LAG-3 (TSR-033), in addition to a bi-specific antibody drug candidate targeting PD-1/LAG-3 (TSR-075).

About TESARO
TESARO is an oncology-focused biopharmaceutical company dedicated to improving the lives of cancer patients by acquiring, developing and commercializing safer and more effective therapeutics. For more information, visit www.tesarobio.com.

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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. Examples of forward-looking statements contained in this press release include, among others, statements regarding the expected timing of initiation, enrollment, data and regulatory submissions related to our various ongoing and planned niraparib clinical trials; and our niraparib clinical development strategy. Forward-looking statements in this release involve substantial risks and uncertainties that could cause our research and development programs, clinical results, regulatory outcomes, and financial and other 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 related to the acceptance of niraparib in the marketplace, competition, the uncertainties inherent in the execution and completion of clinical trials, uncertainties surrounding the timing of availability of data from clinical trials, uncertainties surrounding potential actions by regulatory authorities, uncertainties regarding the expected timing and magnitude of certain expenditures, risks related to manufacturing and supply, risks related to intellectual property, and other matters that could affect our financial results, the results of our ongoing and planned development programs, and/or the availability or commercial potential of our products and drug candidates. 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, 2017.

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[1] Bevacizumab Prescribing Information
[2] NCCN clinical practice guidelines in oncology. Ovarian cancer, including fallopian tube cancer and primary peritoneal cancer. Version 2. 2018. https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf [accessed 03.25.18]
[3] Gelmon, et al. *Lancet Oncol* 2011; Sandhu, et al. *Lancet Oncol* 2013
[4] Fong *J Clin Onocol* 2010, Domchek, et al. *Gyn Oncol* 2016;
[5] Hamanishi, et al. *ASCO* 2015 (some patients had clear cell cancer); Varga, et al. *ASCO* 2017

Primary Logo

Source: TESARO, Inc.