TESARO Summarizes TOPACIO and QUADRA Trial Results Presented at 2018 ASCO Annual Meeting

June 4, 2018

- **TOPACIO data for ZEJULA® (niraparib) in combination with an anti-PD-1 mAb highlight promising activity in platinum-resistant/refractory ovarian cancer and triple-negative breast cancer beyond patients with *BRCA* mutations and support initiation of registration trials**
- **QUADRA results demonstrate durable responses beyond patients with *BRCA* mutations in late-line ovarian cancer treatment setting and support label expansion**
- **Investor webcast to highlight ZEJULA's differentiation in difficult-to-treat ovarian cancer settings and potential in triple-negative breast cancer**

CHICAGO, June 04, 2018 (GLOBE NEWSWIRE) -- **TESARO, Inc.**(NASDAQ:TSRO), an oncology-focused biopharmaceutical company, summarized the results of the TOPACIO and QUADRA trials during an investor briefing held in conjunction with the 2018 American Society of Clinical Oncology (ASCO) Annual Meeting.

"The promising data presented at this year's ASCO meeting demonstrated the potential of ZEJULA not only as a monotherapy treatment for women with advanced ovarian cancer, but also in combination with an anti-PD-1 antibody, to provide a meaningful clinical benefit to patients beyond those with *BRCA* mutations," said Mary Lynne Hedley, Ph.D., President and COO of TESARO. "Our oncology development strategy is focused on rational therapeutic combinations and niraparib and TSR-042, our anti-PD-1 antibody, are the foundation of this strategy. The TOPACIO results support the advancement of combination studies in ovarian cancer and breast cancers and we have initiated preparations for registrational trials of niraparib in combination with TSR-042 in these settings. QUADRA results demonstrated that ZEJULA is active as a late-line treatment for patients beyond those with *BRCA* mutations, which is the only treatment setting in which PARP inhibitors are approved today, and we intend to submit an sNDA in the fourth quarter of 2018."

TOPACIO Data Demonstrate Encouraging Activity of Niraparib in Combination with anti-PD-1 in Platinum-Resistant/Refractory Ovarian Cancer

Prior clinical studies have shown that monotherapy with PARP inhibitors or anti-PD-1 antibodies has limited efficacy in the treatment of patients with platinum-resistant/refractory ovarian cancer or triple-negative breast cancer beyond those patients with *BRCA* mutant tumors, and these patients generally face a poor prognosis. 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/refractory ovarian cancer or triple-negative breast cancer (TNBC). Following dose finding in Phase 1, niraparib was administered orally, once-daily, at a dose of 200 milligrams in combination with 200 milligrams of pembrolizumab administered intravenously on day one of each 21-day treatment cycle in two patient cohorts: platinum-resistant or refractory ovarian cancer and TNBC. Endpoints included objective response rate (ORR), duration of response (DOR) and disease control rate (DCR; CR+PR+SD).

At the time of data cutoff, of the 62 patients enrolled with ovarian cancer, 60 were evaluable for an initial response assessment. The population had been treated with a median of 2 (range of 1 to 5) prior lines of therapy; 50% had platinum-resistant ovarian cancer, 29% were platinum-refractory, 63% had received prior bevacizumab, and 21% were platinum ineligible. Data indicate an ORR (CR and PR) of 25% and a DCR of 67% in the evaluable population; ORR in the *BRCA*mut cohort was 25% with a DCR of 63%; ORR in the *BRCA*wt cohort was 24% with a DCR of 65%. Response rates were not dependent on biomarker status or platinum status. ORR was 23% (7/30) in platinum-resistant ovarian cancer patients, 24% (4/17) in platinum-refractory patients and 31% (4/13) in patients who were platinum ineligible per investigator's assessment (typically due to prior platinum hypersensitivity, toxicities or other reasons that platinum could not be tolerated). Median DOR was 9.3 months, with 9 patients remaining on treatment. The most common grade ? 3 adverse events (AEs) included anemia (21%) and thrombocytopenia (9%) at a 200-milligram starting dose of niraparib. Following a successful discussion with FDA, a registration study with TSR-042 plus niraparib is being planned.

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].

TOPACIO Results in Advanced Triple-Negative Breast Cancer Show Encouraging Activity of Niraparib in Combination with anti-PD-1

At the time of data cutoff, of the 55 patients enrolled with TNBC, 46 were available for an initial response assessment, 15 of whom had *BRCA* mutations and 5 of whom were HRRmut. In the TNBC population evaluable for initial response assessment, ORR was 28% and DCR was 50%, while in the *BRCA*mut population, ORR was 60% and DCR was 80%, with mPFS of 8.3 months. In the combined *BRCA*mut plus HRRmut population, ORR was 55% and DCR was 80%, with mPFS of 6.4 months. Median DOR has not been reached with 62% (8/13) of responders remaining on treatment, including five patients with long-term, ongoing clinical benefit for approximately one year. The combination was well tolerated with the most commonly observed grade ? 3 AEs including anemia (15%) and thrombocytopenia (13%). Of note, the incidence of thrombocytopenia was substantially reduced with the 200-milligram dose of niraparib in both the ovarian cancer and TNBC cohorts in comparison to what has been observed in clinical trials with a starting dose of 300 milligrams niraparib. Following a successful discussion with FDA, a registration study of niraparib plus TSR-042 is being planned.

For patients with TNBC, the standard of care is chemotherapy[6], which generally results in a median PFS in the range of three to five months, and median overall survival of ? 12 months[7]. PARP inhibitor monotherapy has demonstrated clinical activity in TNBC patients who are germline *BRCA* mutation carriers, but has not shown activity in breast cancer beyond g*BRCA*mut patients[8]. Anti-PD-1 antibody monotherapy has demonstrated modest activity in previously treated PD-1L positive TNBC, with an ORR of approximately 5-18% and median PFS of approximately two months[9].

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.

QUADRA Results Demonstrate Durable Potential of ZEJULA in Late-Line Ovarian Cancer Setting Beyond Patients with *BRCA* Mutations

Previous studies have shown that meaningful activity of other PARP inhibitors in the late-line treatment of ovarian cancer is limited to populations with *BRCA* mutations. Efficacy of cytotoxic chemotherapy is limited in patients with heavily-pretreated ovarian cancer. QUADRA, a single arm study (n=463), was conducted to assess the activity of ZEJULA monotherapy in the fourth-line or greater treatment of patients with ovarian cancer, regardless of platinum or biomarker status. In QUADRA, less than 20% of patients had a *BRCA* mutation, 27% received niraparib as a sixth or later line therapy, two-thirds were platinum resistant or refractory (33% and 35%, respectively), and 48% were HRD positive. The majority of platinum sensitive patients who enrolled in QUADRA were considered platinum ineligible, and 62% had received prior bevacizumab. The median time from last chemotherapy until the first dose of niraparib was two months.

The primary efficacy population included fourth or fifth line patients who were previous PARPi naïve, platinum sensitive, and HRD positive (n= 45). The ORR in this population was 29% (95% CI 16-44, p=0.0003). Approximately one-third of patients (27%) enrolled in QUADRA were treated in the sixth or later line of therapy. For patients who were fourth or later line, HRD-positive and platinum sensitive (n=51), the ORR was 27%, the disease control rate (DCR; CR + PR + SD) was 69%, and DOR was 9.2 months. Among those treated in fourth or later line of therapy, clinical benefit (CR+PR+SD) rate for at least 16 weeks was 53% for patients with a *BRCA* mutation and 49% for patients who were HRD positive and platinum sensitive. Responses to niraparib were durable, with a median DOR of 9.4 months across the entire evaluable patient population. An estimated 44% of all responses lasted 12 months or more.

Median overall survival (OS) in all patients treated fourth line or later was 17.2 months. Median OS was 16.6 months in HRD-negative or unknown patients, 19.0 months in HRD-positive patients and 26.0 months in patients with *BRCA* mutations.

At a starting dose of 300 milligrams of ZEJULA, the most commonly observed grade 3 or higher adverse events were consistent with prior clinical experience and included anemia (26.3%) and thrombocytopenia (20.5%), which were generally managed via dose modifications. TESARO intends to submit a sNDA to FDA in the fourth quarter of 2018.

Investor Briefing and Webcast
TESARO will host an investor and analyst briefing in Chicago on Monday, June 4 at 6:15PM local time in conjunction with the ASCO Annual Meeting. A reception will begin at 6:00PM CT, preceding the presentation. During this briefing, TESARO management will provide a business overview and pipeline update and will answer questions from investors and analysts. This event will be webcast live and archived for 30 days, and may be accessed from the TESARO Investor Events and Presentations webpage at www.tesarobio.com.

About the QUADRA Clinical Trial
QUADRA is an open-label, single arm trial designed to evaluate the safety and efficacy of ZEJULA in the treatment setting of ovarian cancer. Patients were enrolled and received a starting dose of 300 milligrams of niraparib once per day. The primary endpoint of this study was objective response rate (ORR) per RECIST in the fourth and fifth-line HRD positive patients who were PARP inhibitor naïve, and platinum sensitive. Other endpoints include durability of response, disease control rate, progression free survival (PFS), overall survival (OS) and safety and tolerability.

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

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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 our development and regulatory plans and expected timelines for such regulatory filings. Forward-looking statements in this release involve substantial risks and uncertainties that could cause our research and development programs, future 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, the uncertainties inherent in the execution and completion of clinical trials, uncertainties surrounding the timing of availability of data from clinical trials, uncertainties surrounding our ongoing discussions with and potential actions by regulatory authorities, risks related to manufacturing and supply, risks related to intellectual

property, and other matters that could affect the availability or commercial potential of our products and product candidates. TESARO undertakes no obligation to update or revise any forward-looking statements. 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, and its Quarterly Report on Form 10-Q for the quarter ended March 31, 2018.

[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 Oncol* 2010, Domchek, et al. *Gyn Oncol* 2016;
[5] Hamanishi, et al. *ASCO* 2015 (some patients had clear cell cancer); Varga, et al. *ASCO* 2017
[6] Bianchini G et al. *Nat Rev Clin Oncol*. 2016 Nov;13(11):674-690; Foulkes WD et al. *N Engl J Med*. 2010 Nov 11;363(20):1938-48.
[7] Kim SB et al. *Lancet Oncol*. 2017 Oct;18(10):1360-1372; O'Shaughnessy et al. *J Clin Oncol*. 2017; Dec 1;32(34):3840-7.
[8] Robson M et al. *N Engl J Med*. 2017 Aug 10;377(6):523-533.
[9] Nanda R et al. *J Clin Oncol*. 2016 Jul 20;34(21):2460-7; Adams S et al. *J Clin Oncol*. 2017;35 (suppl 15):1008; ASCO 2017 Olympiad presentation

Primary Logo

Source: TESARO, Inc.