TESARO Announces Data Presentations at ESMO 2018 Congress

October 20, 2018

- **Data presented indicate that TSR-042 (anti-PD-1 antibody) is well tolerated and has robust activity in patients with MSI-H endometrial cancer**
- **PRIMA safety data for individualized niraparib dose regimen presented**
- **Top-line results for PRIMA trial of niraparib in first-line ovarian cancer regardless of biomarker status expected in late 2019**

MUNICH, Germany, Oct. 20, 2018 (GLOBE NEWSWIRE) -- TESARO, Inc. (NASDAQ: TSRO), an oncology-focused biopharmaceutical company, today summarized updated Phase 1 GARNET data of TSR-042 (anti-PD-1 antibody) in patients with recurrent or advanced microsatellite instability high (MSI-H) endometrial cancer presented during the European Society for Medical Oncology (ESMO) Congress. Blinded, pooled interim safety data from the Phase 3 PRIMA trial of niraparib in patients with first-line ovarian cancer regardless of biomarker status were also presented in a poster discussion session and additional data from the QUADRA trial of niraparib for treatment of late-line ovarian cancer beyond *BRCA*mut were presented in a poster display.

“The updated results from GARNET presented at ESMO demonstrate robust clinical activity of TSR-042 in patients with MSI-H endometrial tumors,” said Mary Lynne Hedley, Ph.D., President and COO of TESARO. “In addition, blinded, pooled interim safety data from the ongoing PRIMA study of niraparib as maintenance therapy in first line ovarian cancer demonstrated a favorable tolerability profile for niraparib when dosed according to a patient’s weight and platelet count compared to a fixed starting dose. These prospective data confirmed that adverse events are reduced for patients starting niraparib at an individualized dose, including a reduction in symptomatic events that are particularly meaningful to patients. We look forward to announcing top-line results for the PRIMA study in late 2019.”

TSR-042 (anti-PD-1 antibody)

GARNET: Efficacy data indicates robust activity of TSR-042 in patients with MSI-high endometrial cancer
GARNET is a multicenter, open-label, Phase 1 dose-escalation study designed to assess the safety, pharmacokinetics, pharmacodynamics, and clinical activity of TSR-042 in patients with advanced solid tumors. The weight-based dose escalation and fixed-dose safety portions of the GARNET study have been completed. The ongoing cohort expansion portion of GARNET is evaluating TSR-042 at a dose of 500 milligrams every 3 weeks (Q3W) for the first 4 cycles, and 1000 milligrams every 6 weeks (Q6W) thereafter in four cohorts: MSI-H endometrial cancer, MSI-H non-endometrial cancer, MSS endometrial cancer and non-small cell lung cancer (NSCLC). Data presented at ESMO included safety and efficacy data from the cohort of patients with MSI-H endometrial cancer.

At the time of data cutoff, 35 patients with MSI-H endometrial cancer had received treatment with TSR-042. Among the 25 patients with MSI-H endometrial cancer who had at least one post-baseline tumor assessment, one had a complete response and 12 had partial responses (including 1 unconfirmed response) by immune related RECIST (irRECIST) criteria (ORR 52%). Twelve of the 13 responses are ongoing (92%), including three patients with partial responses who have thus far received over 60 weeks of treatment with TSR-042. Three additional patients (12%) had stable disease. Median duration of response was not reached.

Preliminary safety findings among the 35 MSI-H endometrial patients indicate TSR-042 is generally well-tolerated. Grade ≥3 treatment-related treatment-emergent adverse events (TEAEs) were reported in 4 out of 35 patients (11.4%).

The data support the unique and convenient dose of TSR-042 of 500 mg Q3W for the first 4 doses, then 1000 mg Q6W thereafter. At this dose, TSR-042 maintained serum concentrations required to retain maximum receptor occupancy throughout the dosing cycle.

The GARNET study is intended to support a Biologics License Application (BLA) submission to the U.S. Food and Drug Administration (FDA) in 2019.

ZEJULA (niraparib)

PRIMA: Prospective validation of individualized niraparib dose regimen based on patient baseline body weight & platelet counts; Rates of adverse events in blinded, pooled patient groups decreased with individualized starting dose compared to fixed starting dose
PRIMA is a double-blind, randomized Phase 3 study designed to evaluate niraparib versus placebo as maintenance therapy in first-line ovarian cancer patients. Platinum responsive patients were initially randomized 2:1 to start niraparib at 300 mg once-daily or placebo and the protocol was subsequently amended to require an individualized starting dose of 200 mg once-daily in patients with baseline weight <77kg or platelet count <150K/μL and 300 mg in all other patients. The trial remains blinded for efficacy and safety.

Among the 727 patients dosed on the study, 480 patients were treated with a fixed 300 mg starting dose of niraparib or placebo and 247 patients were treated with an individualized dose of 300 mg or 200 mg of niraparib based on weight and platelet count or placebo. The findings presented were from evaluable patients with ≥30 days of safety data from blinded pooled niraparib and placebo and indicate improved tolerability with niraparib at the individualized starting dose. TEAEs grade ≥ 3 were lower (36%) in the individualized dosing group (pooled niraparib and placebo) as compared with the group that received a fixed starting dose of 300 mg of niraparib or placebo (52.7%). There were fewer dose reductions and dose discontinuations in patients treated with the individualized starting dose compared with the fixed starting dose. TEAEs leading to treatment discontinuation remained low for both groups at 7.9% for the fixed starting dose and 5.3% for the individualized starting dose group.

The rates of hematologic toxicities of all grades, including grade ≥ 3, were lower with introduction of an individualized starting dose. Grade ≥3 non-hematologic toxicities (nausea, vomiting, fatigue, hypertension, and insomnia) decreased with an individualized starting dose.

QUADRA: Clinical benefit of niraparib treatment demonstrated in late-line ovarian cancer setting, including patients with platinum resistant and refractory disease

Late line ovarian cancer represents a high unmet medical need and efficacy of cytotoxic chemotherapy is limited in patients with heavily-pretreated ovarian cancer. Previous studies have shown meaningful activity of other PARP inhibitors in the late-line treatment of ovarian cancer only in populations with *BRCA* mutations. QUADRA, a single arm study, was conducted to assess the activity of ZEJULA monotherapy in the fourth-line or later treatment of patients with ovarian cancer, regardless of platinum sensitivity or biomarker status.

Niraparib treatment demonstrated durable clinical activity in late-line (≥ 4th line) patients with *BRCA*mut tumors, with an ORR of approximately 30%, including patients with platinum-sensitive, -resistant, and -refractory disease, and a median duration of response of 9.2 months. The clinical benefit rate (CBR; CR+PR+SD) at 16 weeks and 24 weeks were 56% and 38%, respectively. A gradient of clinical activity based on platinum sensitivity was demonstrated in the *BRCA*mut patient population, with greatest activity demonstrated in patients with platinum-sensitive disease (ORR 39%), mOS was not reached (95% CI 19, NE). However, even patients with platinum-resistant and platinum-refractory disease experienced benefit from niraparib treatment with ORR of 33% and 19%, and mOS of 26.0 and 23.3 months, respectively.

Clinical benefit of niraparib extended beyond patients with *BRCA* mutations in this late-line setting. Patients with non-*BRCA*mut/HRDpos platinum-sensitive disease had an ORR of 20%. In total, the biomarker-driven population (*BRCA*mut regardless of platinum status and non-*BRCA*mut HRDpos platinum-sensitive patients) included 98 patients with ORR of 26%, mDOR of 8.3 months, and a mOS of 23.3 months.

The safety profile in the QUADRA treatment study was consistent with the safety profile observed in the NOVA maintenance population.

Details of TESARO's poster presentations are as follows (all times local):

ZEJULA® (niraparib)

Saturday, October 20, 2018, 9:15 AM – 10:45 AM; Lecture time: 9:59 AM

A prospective evaluation of tolerability of niraparib dosing based upon baseline body weight (wt) and platelet (plt) count: Blinded pooled interim safety data from the PRIMA Study

Poster Discussion, Abstract: 941PD, Location: ICM – Room 13, Poster Displayed: Hall B4

Saturday, October 20, 2018, 12:30 PM – 1:30 PM

QUADRA: A phase 2, open-label, single-arm study to evaluate niraparib in patients with relapsed ovarian cancer in 4th or later line of therapy: results from the BRCAmut subset

Poster Session, Abstract: 944P, Location: Hall A3

Saturday, October 20, 2018, 12:30 PM – 1:30 PM

OVARIO: A single-arm, open-label phase 2 study of maintenance therapy with niraparib + bevacizumab in patients with advanced ovarian cancer after response to frontline platinum-based chemotherapy

Poster Session, Abstract: 999TiP, Location: Hall A3

Saturday, October 20, 2018, 12:30 PM – 1:30 PM

Real world occurrence of top three clinical-trial reported adverse events of PARP inhibitor niraparib maintenance therapy in platinum-sensitive recurrent ovarian cancer, a national retrospective observational study of a 200 mg/day starting-dose cohort

Poster Session, Abstract: 986P, Location: Hall A3

Saturday, October 20, 2018, 12:30 PM – 1:30 PM

Brain metastases in primary ovarian cancer: real-world data

Poster Session, Abstract: 946P, Location: Hall A3

TSR-042 (anti-PD-1)

Saturday, October 20, 2018, 9:15 AM – 10:45 AM; Lecture time: 9:15 AM

Preliminary safety, efficacy, and PK/PD characterization from GARNET, a phase 1 clinical trial of the anti–PD-1 monoclonal antibody, TSR-042, in patients with recurrent or advanced MSI-H endometrial cancer

Poster Discussion, Abstract: 935PD, Location: ICM – Room 13, Poster displayed: Hall B4

Niraparib is marketed in the United States and Europe under trade name ZEJULA®.

About ZEJULA (Niraparib)

ZEJULA (niraparib) is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated in the United States and in the EU 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. Important Safety Information Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML), including some fatal cases, was reported in 1.4% of patients receiving ZEJULA vs 1.1% of patients receiving placebo in Trial 1 (NOVA), and 0.9% of patients treated with

ZEJULA in all clinical studies. The duration of ZEJULA treatment in patients prior to developing MDS/AML varied from <1 month to 2 years. All patients had received prior chemotherapy with platinum and some had also received other DNA damaging agents and radiotherapy. Discontinue ZEJULA if MDS/AML is confirmed.

Hematologic adverse reactions (thrombocytopenia, anemia and neutropenia) have been reported in patients receiving ZEJULA. Grade ≥3 thrombocytopenia, anemia and neutropenia were reported in 29%, 25%, and 20% of patients receiving ZEJULA, respectively. Discontinuation due to thrombocytopenia, anemia, and neutropenia occurred, in 3%, 1%, and 2% of patients, respectively. Do not start ZEJULA until patients have recovered from hematological toxicity caused by prior chemotherapy (≤ Grade 1). Monitor complete blood counts weekly for the first month, monthly for the next 11 months of treatment, and periodically thereafter. If hematological toxicities do not resolve within 28 days following interruption, discontinue ZEJULA, and refer the patient to a hematologist for further investigations.

Hypertension and hypertensive crisis have been reported in patients receiving ZEJULA. Grade 3-4 hypertension occurred in 9% of patients receiving ZEJULA vs 2% of patients receiving placebo in Trial 1, with discontinuation occurring in <1% of patients.
ZEJULA can cause fetal harm and females of reproductive potential should use effective contraception.

In clinical studies, the most common adverse reactions (Grades 1-4) in ≥10% of patients included: thrombocytopenia (61%), anemia (50%), neutropenia (30%), leukopenia (17%), palpitations (10%), nausea (74%), constipation (40%), vomiting (34%), abdominal pain/distention (33%), mucositis/stomatitis (20%), diarrhea (20%), dyspepsia (18%), dry mouth (10%), fatigue/asthenia (57%), decreased appetite (25%), urinary tract infection (13%), aspartate aminotransferase (AST)/alanine aminotransferase (ALT) elevation (10%), myalgia (19%), back pain (18%), arthralgia (13%), headache (26%), dizziness (18%), dysgeusia (10%), insomnia (27%), anxiety (11%), nasopharyngitis (23%), dyspnea (20%), cough (16%), rash (21%) and hypertension (20%).

Common lab abnormalities (Grades 1-4) in ≥25% of patients included: decrease in hemoglobin (85%), decrease in platelet count (72%), decrease in white blood cell count (66%), decrease in absolute neutrophil count (53%), increase in AST (36%) and increase in ALT (28%). Please see full U.S. prescribing information, including additional important safety information, available at www.zejula.com.

About GARNET
The ongoing Phase I GARNET trial is evaluating TSR-042 as monotherapy in patients with advanced solid tumors. GARNET included a weight-based dose escalation study (Part 1) and a fixed-dose safety study (Part 2A), both of which have been completed. Results of these studies were used to determine the recommended Phase 2 dose (RP2D; 500 mg Q3W for the first 4 cycles then 1000 mg Q6W). The study is now enrolling patients with MSI-H endometrial cancer, MSI-H non-endometrial cancer, MSS endometrial cancer, and NSCLC into four large expansion cohorts.

About TSR-042

TSR-042 is an investigational humanized anti-programmed death (PD)-1 monoclonal antibody that binds with high affinity to the PD-1 receptor and effectively blocks its interaction with the ligands PD-L1 and PD-L2. TSR-042 is the only anti-PD-1 therapy administered as monotherapy every 3 weeks for 4 doses then every 6 weeks thereafter. TSR-042 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 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 the potential dosing schedule for TSR-042, the expected timing of our clinical trial readouts, and the expected timing of our planned regulatory submission for TSR-042 and niraparib. Forward-looking statements in this release involve substantial risks and uncertainties that could cause our 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 and regulatory submissions, uncertainties surrounding the timing of availability of data from clinical trials, uncertainties surrounding potential actions by regulatory authorities such as the US FDA, risks related to manufacturing and supply, risks related to intellectual property, and other matters that could affect our ongoing and planned development programs, and/or the availability or commercial potential of our products and product candidates, including TSR-042. 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 Quarterly Report on Form 10-Q for the quarter ended June 30, 2018.

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Source: TESARO, Inc.