TESARO

September 11, 2017

TESARO Summarizes ZEJULA and TSR-042 Data Presented at the 2017 ESMO Annual Meeting

MADRID, Spain, Sept. 11, 2017 (GLOBE NEWSWIRE) -- TESARO, Inc. (NASDAQ:TSRO), an oncology-focused biopharmaceutical company, today provided a summary of ZEJULA and TSR-042, an anti-PD-1 antibody, data presented at the 2017 European Society of Medical Oncology (ESMO) Annual Meeting in Madrid.

"ZEJULA is the market-leading PARP inhibitor, with unsurpassed efficacy in a broad patient population and convenient, once-daily dosing," said Mary Lynne Hedley, Ph.D., President and COO of TESARO. "'Watchful waiting' is no longer an acceptable option for women living with ovarian cancer. We believe combination approaches, including niraparib and anti-PD-1 antibodies, will become increasingly important and we are executing on our registration strategy for TSR-042, our anti-PD-1 antibody, in MSI-high cancers."

ZEJULA (niraparib) presentations:

Treatment with niraparib did not impact patient quality of life in the NOVA trial
Quality of life measures are important to understanding the benefit of niraparib in the maintenance treatment setting. Dr. Amit M. Oza, M.D., Senior Staff Physician, Division of Medical Oncology and Hematology, Princess Margaret Cancer Centre, University Health Network, presented quality of life (QoL) data from the Phase 3 ENGOT-OV16/NOVA trial. Patient-reported outcomes (PROs) were evaluated along with individual patient-reported symptoms using the Functional Assessment of Cancer Therapy-Ovarian Symptoms Index (FOSI) and European Quality of Life Scale 5-Dimensions (EQ-5D-5L). The most common PRO symptoms at baseline were fatigue and pain, and 20% of patients experienced nausea at baseline. No significant difference in mean patient-reported outcomes (PRO) scores was observed between patients treated with niraparib versus placebo, regardless of germline *BRCA* mutation status. Hematologic adverse events (thrombocytopenia, neutropenia, anemia) decreased over time with dose modification and did not impact QoL. These results also suggest that patients with ovarian cancer often experience residual symptoms of their disease following the conclusion of chemotherapy.

Safety and efficacy of niraparib in elderly patients comparable to overall population in NOVA
In a poster discussion session, safety and efficacy results from the ENGOT-OV16/NOVA trial were highlighted for a sub-group of elderly patients, aged 70 years and older. In this post-hoc analysis, the efficacy of niraparib was similar for patients aged <70 years compared to patients aged ≥70 years in both the g*BRCA*mut and non-g*BRCA*mut cohorts. Grade ≥3 treatment-emergent adverse events (TEAEs) occurring in >10% of niraparib treated patients were also consistent between the two groups, and dose reductions, interruptions, and treatment discontinuations occurred with similar frequency, regardless of age. These results demonstrate that niraparib may provide clinical benefit to a broad population of patients with ovarian cancer irrespective of age.

Niraparib exposure — response findings support dosing patients at individually adjusted maximal tolerated dose
In a poster discussion session, the relationship between niraparib exposure and efficacy, as well as exposure and safety, was highlighted in patients enrolled in the ENGOT-OV16/NOVA trial. Efficacy as measured by PFS was compared in patients with high exposure (defined as greater than median exposure) versus low exposure (defined as less than or equal to median exposure). Patients experienced similar efficacy at their individual maximum tolerated dose regardless of the dose received. Reaching maximal exposure for individual patients, as was done in the ENGOT-OV16/NOVA trials via dose modifications, was likely an important factor in achieving maximal efficacy, especially for patients without a *BRCA* mutation. Limited exposure-efficacy association was observed among patients who were germline *BRCA* mutation carriers, while the exposure-efficacy association was more apparent for patients who were not germline *BRCA* mutation carriers. On a population level, the incidence of treatment-emergent adverse events (TEAEs) was higher with increased dose. These findings support that patients, especially those with *BRCA* wild-type tumors, should be treated at their individually adjusted maximal tolerated dose to provide the optimal chance of efficacy.

Model highlights niraparib pharmacokinetic properties, including high tissue distribution and slow elimination, and no need for dose adjustments in patients with mild-to-moderate renal or hepatic impairment
In a poster display session, data from the Phase 1 dose-escalation and expansion studies (n=104) and the Phase 3 ENGOT-OV16/NOVA study (n=408) of niraparib were used to model the impact of patient variables (age, race, ethnicity, body weight), renal impairment (normal, mild, or moderate), and hepatic function (baseline serum alanine and aspartate aminotransferase, albumin, total bilirubin) on niraparib pharmacokinetic parameters. In the base model, the typical value for niraparib apparent clearance was 16.2 L/h, with inter-individual variability of 52.6%. The estimated volume of distribution

was 1074 L (290 L central and 784 L peripheral compartment). None of the patient variables impacted niraparib pharmacokinetics, including mild-to-moderate renal impairment and mild hepatic impairment, and model diagnostics showed good agreement between predicted and observed individual niraparib plasma concentrations. These results demonstrate that no dose adjustments are needed for patients treated with niraparib with mild-to-moderate renal or hepatic impairment.

Bevacizumab-niraparib combination demonstrated preliminary evidence of activity and a predictable adverse event profile

Updated data from the ongoing Phase 2 AVANOVA study of bevacizumab plus niraparib, an Investigator Supported Trial (IST), in patients with platinum sensitive recurrent ovarian cancer (n=12) demonstrated activity and a predictable adverse event profile. In the first cycle (21 days) of the study, patients experienced expected and manageable adverse events including anemia, constipation, fatigue, hypertension, nausea and thrombocytopenia. One dose-limiting toxicity (grade 3 thrombocytopenia) was observed at the highest dose level. Three patients were dose reduced and two patients terminated bevacizumab. Preliminary evidence of activity was demonstrated, with a disease control rate of 92% and response rate of 50%, including 1 CR and 5 PRs. There were five additional patients with stable disease. The median progression-free survival (PFS) was 49 weeks. These data support the potential to combine niraparib plus bevacizumab. Part 2 of the AVANOVA trial continues to enroll patients.

Frequent hospitalizations and ER visits during "watchful waiting" period support a change in clinical practice to maintenance therapy options for ovarian cancer patients

A retrospective study was conducted in the U.S. to characterize the treatment-free interval (or "watchful waiting") for patients newly diagnosed with ovarian cancer following completion of treatment with platinum-based chemotherapy. The analysis found that during the "watchful waiting" period, 30.1% of patients were admitted to the hospital as an in-patient, and 27.4% of patients visited the emergency room. These results suggest that patients with ovarian cancer often experience residual symptoms of their disease following the conclusion of chemotherapy.

Preliminary Phase 2 niraparib/pembrolizumab combination (TOPACIO) data shows activity in patients with platinum-resistant ovarian and triple-negative breast cancer

Data from a Phase 1 dose-escalation study of niraparib in combination with pembrolizumab in patients with platinum-resistant ovarian cancer (OC) or triple negative breast cancer (TNBC) was presented, along with preliminary response data from patients thus far treated in the Phase 2 TOPACIO study. In Phase 1, among the nine evaluable OC patients, five responded (partial or complete response) and four achieved stable disease. Three of the five responders had tumors that tested as wildtype *BRCA* 1/2 and three as PD-L1 negative (<1%). Of the four evaluable TNBC patients, three had stable disease and one patient came off study prior to her first assessment. The most common treatment related grade ≥3 adverse events occurring in ≥2 patients included anemia (35.7%), thrombocytopenia (35.7%), neutropenia (14.3%) and decreased platelet counts (14.3%). The recommended Phase 2 dose of niraparib was established as 200 mg oral niraparib once daily (increasing to 300 mg after cycle 2 in patients with no significant hematologic toxicities) in combination with 200 mg IV pembrolizumab on day 1 of each 21-day cycle.

The Phase 2 portion of the TOPACIO study is ongoing, and, as of the data cutoff, 36 OC patients and 47 TNBC patients were enrolled out of a planned 48 patients for each tumor cohort. Twenty-nine OC and 27 TNBC patients have been assessed by at least one scan with responses observed in both *BRCA* wild-type and PD-L1 negative tumors. Among the patients who had received at least one on-study scan, 6 OC patients and 5 TNBC patients had a ≥30% decrease in tumor lesion size and 10 of these 11 patients continue on therapy. Overall 52% OC and 63% TNBC patients who did not have progressive disease continue on therapy. No new safety signals were identified, and less than 7% of Phase 2 patients had experienced grade ≥3 thrombocytopenia during the first treatment cycle. Thirty patients (36.1%) enrolled in Phase 2 reported treatment-related grade ≥3 adverse events including anemia (8.4%), fatigue (6.0%), platelet count decrease (6.0%) and thrombocytopenia (6.0%).

<u>TSR-042 (anti-PD-1 antibody)</u>

TSR-042 safety profile and clinical activity demonstrated in heavily pre-treated patients

In a poster display session, preliminary safety, efficacy, receptor occupancy, and pharmacokinetic data for TSR-042, an anti-PD-1 antibody, were presented from a two-part Phase 1 study. No dose limiting toxicities were observed. Adverse events included fatigue, nausea, arthralgia, decreased appetite, and pruritus, which occurred in ≥10% of patients. In Part 1 (n=21), two patients with ovarian cancer and small cell lung cancer who were treated with TSR-042 experienced a partial response and five patients with fallopian tube or ovarian cancer had stable disease, two of whom are continuing treatment. Consistent with data reported for other anti-PD-1 antibodies, maximum direct and functional receptor occupancy was observed with both CD3+ binding and IL-2 stimulation assays at all three dose levels evaluated. In Part 2A (n=13), full receptor occupancy, as assessed by the assays used in Part 1, was maintained over 3 and 6 weeks at doses of 500 mg and 1,000 mg, respectively.

These preliminary findings indicate that TSR-042 is safe and well tolerated, with a safety and efficacy profile expected for an agent targeting the PD-1 pathway, evidence of linear PK, and sustained target engagement at administration intervals up to 6 weeks. The recommended Phase 2 dose was established at 500 mg Q3W for the first four cycles and 1000 mg Q6W

thereafter. Serum concentrations of TSR-042 observed 3 weeks after the 500 mg dose were comparable to those observed 6 weeks after the 1000 mg dose. Patients with microsatellite instability high (MSI-H) and microsatellite stable endometrial cancer and non-small cell lung cancer are currently enrolling in the expansion phase of this study, and additional tumor types are planned for evaluation.

About ZEJULA® (Niraparib)

Niraparib is marketed in the United States 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 all 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.

In clinical studies, the most common adverse reactions included: thrombocytopenia, anemia, neutropenia, nausea, constipation, vomiting, abdominal pain/distension, mucositis/stomatitis, diarrhea, fatigue/asthenia, decreased appetite, headache, insomnia, nasopharyngitis, dyspnea, rash and hypertension.

Please see full Prescribing Information for additional Safety Information at www.zejula.com.

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.

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.

Investor/Media Contact:
Jennifer Davis
Vice President, Corporate Communications & Investor Relations
+1.781.325.1116 or jdavis@tesarobio.com