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# TESARO ANNOUNCES U.S. FDA APPROVAL OF VARUBI® IV FOR DELAYED NAUSEA AND VOMITING ASSOCIATED WITH CANCER CHEMOTHERAPY

- VARUBI injectable emulsion features a ready-to-use, single-dose vial for intravenous administration
- Availability of new formulation offers healthcare providers the flexibility to choose oral or IV administration
- VARUBI provides enhanced control of delayed CINV as part of an antiemetic regimen, particularly for patients receiving cisplatin, carboplatin or anthracycline/cyclophosphamide-based chemotherapy
- U.S. commercial launch planned for November

WALTHAM, MA, October 25, 2017 – TESARO, Inc. (NASDAQ: TSRO), an oncology-focused biopharmaceutical company, today announced that the U.S. Food and Drug Administration (FDA) has approved VARUBI® (rolapitant) IV in combination with other antiemetic agents in adults for the prevention of delayed nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy. Delayed nausea and vomiting can occur anytime between 25 and 120 hours following chemotherapy, and is often extremely debilitating.

VARUBI is a highly selective and competitive antagonist of human substance P/neurokinin 1 (NK-1) receptors, which play an important role in the delayed phase of chemotherapy-induced nausea and vomiting (CINV). With a long plasma half-life of approximately seven days, a single dose of VARUBI, as part of an antiemetic regimen, significantly improved complete response (CR) rates in the delayed phase of CINV. Results from three Phase 3 trials of VARUBI oral tablets demonstrated a significant reduction in episodes of vomiting or use of rescue medication during the 25- to 120-hour period following administration of highly emetogenic and moderately emetogenic chemotherapy regimens. In addition, patients who received VARUBI reported experiencing less nausea that interfered with normal daily life and fewer episodes of vomiting or retching over multiple cycles of chemotherapy. Results from a bioequivalence trial demonstrated comparability of the IV and oral formulations of VARUBI.

VARUBI IV is supplied in ready-to-use vials and does not require refrigerated storage or mixing. As a result, utilization in busy chemotherapy clinics is straightforward and easily adopted into existing practice patterns for administration of antiemetic regimens associated with emetogenic chemotherapy. VARUBI IV is to be administered up to two hours before chemotherapy administration in combination with a 5-$HT_3$ receptor antagonist and dexamethasone. No dosage adjustment is required for dexamethasone, a CYP3A4 substrate, and VARUBI is the first intravenously administered NK-1 receptor antagonist approved by the FDA that does not contain polysorbate 80.

"The approval of VARUBI IV represents a significant milestone for TESARO. The majority of NK-1 receptor antagonist doses are administered intravenously in the U.S., and with the introduction of VARUBI IV, we now offer healthcare providers a unique, easy-to-use option that fits well into standard operating practices of a chemotherapy clinic or hospital," said Mary Lynne Hedley, Ph.D., President and COO of TESARO. "We will continue our efforts to expand awareness of delayed chemotherapy-induced nausea and vomiting, and plan to make this important medicine available next month."

"Many healthcare providers tend to believe that CINV is no longer an unmet need but the reality is that more than half of patients treated with emetogenic chemotherapy experience delayed CINV, even when prescribed standard preventative therapies, such as a 5-$HT_3$ receptor antagonist and dexamethasone," said Lee Schwartzberg, M.D., Professor of Medicine at University of Tennessee Health Science Center. "The FDA approval of VARUBI IV gives doctors and nurses a new option to help protect their patients from these often preventable side effects."

The full prescribing information for VARUBI IV will be available at www.VarubiRx.com.

**TOGETHER with TESARO™**

TOGETHER with TESARO™ is a patient resource program dedicated to supporting people living with cancer. The program assists with access issues, so that patients with cancer can be free to focus on treatment goals and simply living life. It provides a full suite of services to meet each patient's needs and individual experience. A team of access and affordability experts is available to help oncology practices and patients gain access to the medication they require. TOGETHER with TESARO will continue to evolve and grow to meet provider and patient needs.

For more information, please visit www.togetherwithtesaro.com or call 1-844-2TESARO (1-844-283-7276).

**About Chemotherapy-Induced Nausea and Vomiting (CINV)**

Chemotherapy-induced nausea and vomiting is a debilitating, yet often preventable side effect of chemotherapy. Up to 50% of patients undergoing highly or moderately emetogenic chemotherapy experience delayed CINV (25 to 120 hours post chemotherapy) — even when prescribed a 5-$HT_3$ receptor antagonist and corticosteroid. Blocking both 5-$HT_3$ and NK-1 receptors has been shown to offer better control of nausea and vomiting than inhibiting 5-$HT_3$ receptors alone. Adding a single dose of VARUBI to an antiemetic regimen, including a 5-$HT_3$ receptor antagonist and corticosteroid, further improves prevention of CINV in the delayed phase following chemotherapy.

**About the VARUBI (Rolapitant) Clinical Program**

The superior efficacy of VARUBI was established in multiple global randomized, well-controlled, double-blinded clinical trials that enrolled more than 2,500 patients. VARUBI, when administered in combination with a 5-$HT_3$ receptor antagonist and dexamethasone, was superior to a 5-$HT_3$ receptor antagonist and dexamethasone alone in preventing delayed CINV in patients receiving either moderately or highly emetogenic chemotherapy.

The clinical profile of VARUBI in cisplatin-based highly emetogenic chemotherapy (HEC) was confirmed in two identical Phase 3 studies: HEC1 and HEC2. Both trials met their primary endpoint

of complete response (CR), and demonstrated statistical superiority of rolapitant (180 mg oral) compared to active control (5-$HT_3$ receptor antagonist plus dexamethasone) in the delayed phase (25–120 hours) of CINV. In HEC1, 264 patients received rolapitant and 262 received active control. The proportion of patients achieving a CR was 72.7% vs. 58.4% (p=<0.001). In HEC2, 271 patients received rolapitant and 273 received active control. The proportion of patients achieving a CR was 70.1% vs. 61.9% (p=0.043). The most common adverse reactions (≥3%) among patients receiving cisplatin-based chemotherapy were neutropenia (9% VARUBI vs. 8% control), hiccups (5% vs. 4%), and abdominal pain (3% vs. 2%).

A Phase 3 trial was also conducted to evaluate rolapitant (180 mg oral) compared to active control in 1,332 patients receiving moderately emetogenic chemotherapy regimens, including anthracycline/cyclophosphamide combinations, carboplatin, irinotecan, pemetrexed, oxaliplatin, and doxorubicin. This trial met its primary endpoint of CR, and demonstrated statistical superiority of rolapitant compared to active control (5-$HT_3$ receptor antagonist plus dexamethasone) in the delayed phase of CINV. The proportion of patients achieving a CR was 71.3% vs 61.6% (p=<0.001). The most common adverse reactions (≥3%) among patients receiving these chemotherapies were decreased appetite (9% VARUBI vs. 7% control), neutropenia (7% vs. 6%), dizziness (6% vs. 4%), dyspepsia (4% vs. 2%), urinary tract infection (4% vs. 3%), stomatitis (4% vs. 2%), and anemia (3% vs. 2%).

Primary data from the three Phase 3 studies have been published in *Lancet Oncology*, the analysis of the non-AC MEC population was presented at the 2015 annual meeting of the Multinational Association for Supportive Care in Cancer, and commentary has been provided in *Nature Reviews Clinical Oncology*.

In addition to the Phase 3 program, a bioequivalence study was conducted in healthy volunteers to compare the exposure of the 166.5 milligram dose of IV rolapitant to the exposure of a 180 milligram dose of oral rolapitant. Study participants were randomized to receive a single dose of either 166.5 milligrams of intravenous rolapitant administered over 30 minutes (n=61) or 180 milligrams of oral rolapitant (n=62). The primary endpoint of this pivotal study was bioequivalence, defined by estimating whether the 90% confidence intervals (CI) for the ratio of the area under the curves (AUCs) of the two formulations are entirely included within the acceptance range of 80% to 125%. Safety and tolerability were also assessed for both formulations. The safety profile was consistent with previous clinical trials with oral rolapitant, except for infusion-site reactions observed with the IV formulation.

**VARUBI Additional Safety Information**

VARUBI is contraindicated in patients taking CYP2D6 substrates with a narrow therapeutic index, such as thioridazine and pimozide. VARUBI can significantly increase the plasma concentrations of thioridazine and pimozide, which may result in QT prolongation and Torsades de Pointes.

VARUBI is a moderate inhibitor of CYP2D6 and significantly increases the plasma concentrations of CYP2D6 substrates for at least 28 days, with inhibitory effects expected to persist for an unknown duration. Monitor for adverse reactions when VARUBI is coadministered with CYP2D6 substrates without a narrow therapeutic index (avoid coadministration with CYP2D6 substrates with a narrow therapeutic index, thioridazine and pimozide; see Contraindication).

In clinical trials, the most common adverse reactions reported were neutropenia, hiccups, decreased appetite and dizziness. IV administration of VARUBI was also associated with infusion-related symptoms (e.g., sensation of warmth, abdominal pain, dizziness, and paresthesia).

Avoid use of VARUBI in patients who require chronic administration of strong CYP3A4 inducers (e.g., rifampin), as significantly reduced plasma concentrations of VARUBI can decrease the efficacy of VARUBI.

VARUBI, administered as an IV or oral medication, is not an inhibitor of CYP3A4 and no dose adjustment is required for co-administered CYP3A4 substrates, including dexamethasone.

VARUBI IV did not inhibit breast cancer resistance protein (BCRP) and P-glycoprotein (P-gp). VARUBI given as an oral dose is an inhibitor of breast cancer resistance protein (BCRP) and P-glycoprotein (P-gp). Increased plasma concentrations of BCRP substrates (e.g., methotrexate, topotecan, or irinotecan) and P-gp substrates (e.g., digoxin) with a narrow therapeutic index may result in potential adverse reactions. Monitor digoxin concentrations with concomitant use of VARUBI, and adjust the dosage as needed to maintain therapeutic concentrations.

Monitor INR and prothrombin time and adjust the dosage of warfarin, as needed, to maintain target INR.

VARUBI is available by prescription only. Please see full prescribing information, including additional important safety information, available at www.varubirx.com.

**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.

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**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. Examples of forward-looking statements contained in this press release include, among others, statements regarding the expected timing of the launch of VARUBI IV in the United States. Forward-looking statements in this release involve substantial risks and uncertainties that could cause 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 related to manufacturing and supply, risks related to competition, and other matters that could affect the availability or commercial potential of VARUBI IV. 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 June 30, 2017.

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