November 16, 2015

OPKO Licensee TESARO Announces the Launch of VARUBI(TM) (Rolapitant) in the United States

- VARUBI™(rolapitant) provides extended protection for chemotherapy-induced nausea and vomiting (CINV) in the delayed phase (25-120 hours) with a single dose as part of an antiemetic regimen
- More than half of patients undergoing emetogenic chemotherapy may experience delayed CINV, even when prescribed a 5-HT_3 receptor antagonist and a corticosteroid

MIAMI--(BUSINESS WIRE)-- OPKO Health Inc. (NYSE: OPK), today announced that VARUBI™ (rolapitant), an NK-1 receptor antagonist, is now available in the United States. The U.S. Food and Drug Administration (FDA) approved VARUBI on Sept. 1, 2015, for use 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.

VARUBI is a selective and competitive antagonist of human substance P/neurokinin 1 (NK-1) receptors, with a plasma half-life of approximately seven days. Results from all three Phase 3 trials of VARUBI demonstrated that patients receiving highly and moderately emetogenic chemotherapy agents, including platinum and anthracycline/cyclophosphamide-containing regimens, experienced a significant reduction in episodes of vomiting or use of rescue medication during the 25 to 120 hour period following chemotherapy administration. 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. No dosage adjustment is required for dexamethasone, a CYP3A4 substrate, when administering VARUBI. A single dose (two 90 milligram tablets) of VARUBI is to be administered approximately one to two hours prior to chemotherapy administration, in combination with a 5-HT_3 receptor antagonist and dexamethasone.

Just three weeks after the approval of VARUBI by the U.S. FDA, the National Comprehensive Cancer Network (NCCN) added VARUBI to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Antiemesis Version 2.2015 as a recommended option, in combination with other antiemetic agents, for patients receiving both high emetic risk intravenous chemotherapy (HEC) and moderate emetic risk intravenous chemotherapy (MEC). Category 1, the highest level category of evidence and consensus, was granted to VARUBI for both HEC and MEC chemotherapy.

The full prescribing information for VARUBI is available at www.VarubiRx.com.

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 VARUBI™

VARUBI is a substance P/neurokinin-1 (NK-1) receptor antagonist indicated 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. NK-1 receptors are highly concentrated in the brain and bind neurokinin substance P. Activation of NK-1 receptors plays a central role in nausea and vomiting induced by emetogenic stimuli, including certain cancer chemotherapies. A Positron Emission Tomography (PET) study with rolapitant in normal, healthy volunteers demonstrated that rolapitant crosses the blood brain barrier and occupies brain NK-1 receptors at high levels for up to 120 hours. VARUBI has a half-life of approximately seven days, which may contribute to the ability of a single dose of VARUBI to cover the entire delayed CINV phase (25-120 hours).

An intravenous formulation of rolapitant is also being developed. TESARO licensed exclusive rights for the development, manufacture, commercialization, and distribution of VARUBI (rolapitant) from OPKO Health, Inc.

About the VARUBI (Rolapitant) Clinical Program

The superior efficacy of VARUBI was established in multiple global, randomized, well-controlled, 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 significantly superior to a 5-HT_3 receptor antagonist and dexamethasone 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) in the delayed phase (25-120 hours) of CINV and demonstrated statistical superiority of rolapitant 180 mg compared to active control (5-HT_3 receptor antagonist + dexamethasone). In HEC1, 264 patients received rolapitant 180 mg, and 262 received 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 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 compared to active control in 1,332 patients receiving anthracycline/cyclophosphamide combinations or moderately emetogenic chemotherapy regimens, including carboplatin, irinotecan, pemetrexed, oxaliplatin, and doxorubicin. This trial met its primary endpoint of CR in the delayed phase of CINV and demonstrated statistical superiority of rolapitant 180 mg compared to active control (5-HT_3 receptor antagonist + dexamethasone). 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 for the Multinational Association for Supportive Care in Cancer, and commentary has been provided in *Nature Reviews Clinical Oncology*.

Indication and Important Safety Information for VARUBI™ (Rolapitant)

Indication

VARUBI, in combination with other antiemetic agents, is indicated 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.

Contraindication

VARUBI is contraindicated in patients receiving thioridazine, a CYP2D6 substrate. A significant increase in plasma concentrations of thioridazine may result in QT prolongation and Torsades de Pointes.

Warnings and precautions

Interaction with CYP2D6 substrates with a narrow therapeutic index

- The inhibitory effect of VARUBI on CYP2D6 lasts for at least 7 days and may last longer after administration of a single dose of VARUBI.
- Avoid use of VARUBI in patients who are receiving pimozide, a CYP2D6 substrate. An increase in plasma concentrations of pimozide may result in QT prolongation.
- Monitor for adverse reactions if concomitant use of VARUBI and other CYP2D6 substrates with a narrow therapeutic index cannot be avoided.

Adverse reactions

- In patients receiving cisplatin-based, highly emetogenic chemotherapy in cycle 1, the most common adverse reactions reported at an incidence of ≥5% and a frequency greater than control were neutropenia (9% VARUBI vs 8% control) and hiccups (5% vs 4%).
- In patients receiving moderately emetogenic chemotherapy and combinations of anthracycline and cyclophosphamide in cycle 1, the most common adverse reactions

reported at an incidence of ≥5% and a frequency greater than control were decreased appetite (9% VARUBI vs 7% control), neutropenia (7% vs 6%), and dizziness (6% vs 4%).

Drug interactions

- VARUBI is an inhibitor of breast cancer resistance protein (BCRP) and P-glycoprotein (P-gp). Increased plasma concentrations of BCRP and P-gp substrates with a narrow therapeutic index may result in potential adverse reactions. Monitor for adverse reactions related to the concomitant drug if use with VARUBI cannot be avoided
- 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 is available by prescription only.

About OPKO Health

OPKO Health, Inc. is a diversified healthcare company that seeks to establish industry-leading positions in large, rapidly growing markets. Our diagnostics business includes Bio-Reference Laboratories, the nation's third-largest clinical laboratory with a core genetic testing business and a 420-person salesforce to drive growth and leverage new products, including the 4Kscore® prostate cancer test and the Claros®1 in-office immunoassay platform. Our pharmaceutical business features Rayaldee™, a treatment for secondary hyperparathyroidism in stage 3-4 chronic kidney disease patients with vitamin D deficiency (March 29, 2016 PDUFA date) and VARUBI™ for chemotherapy-induced nausea and vomiting (oral formulation approved by FDA and pending launch by partner Tesaro, IV formulation in Phase 3). Our biologics business includes hGH-CTP, a once-weekly human growth hormone injection (in Phase 3 and partnered with Pfizer), and a long-acting Factor VIIa drug for hemophilia (entering Phase 2a). We also have production and distribution assets worldwide, multiple strategic investments and an active business development strategy. More information is available at www.opko.com.

SAFE HARBOR STATEMENT

This press release contains "forward-looking statements," as that term is defined under the Private Securities Litigation Reform Act of 1995 (PSLRA), which statements may be identified by words such as "expects," "plans," "projects," "will," "may," "anticipates," "believes," "should," "intends," "estimates," and other words of similar meaning, including statements regarding the commercial availability of VARUBI in the U.S. and TESARO's plans to develop and commercialize additional therapies, as well as other non-historical statements about our expectations, beliefs or intentions regarding our business, technologies and products, financial condition, strategies or prospects. Many factors could cause our actual activities or results to differ materially from the activities and results anticipated in forward-looking statements. These factors include those described in our filings with the Securities and Exchange Commission, as well as the risks inherent in funding, developing and obtaining regulatory approvals of new, commercially-viable and competitive products and treatments. In addition, forward-looking statements may also be adversely affected by general market factors, competitive product development, product availability, federal and state regulations and legislation, the regulatory process for new

products and indications, manufacturing issues that may arise, patent positions and litigation, among other factors. The forward-looking statements contained in this press release speak only as of the date the statements were made, and we do not undertake any obligation to update forward-looking statements. We intend that all forward-looking statements be subject to the safe-harbor provisions of the PSLRA.

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