# AVEO Oncology Presents Three Posters for Tivozanib at the 2022 ASCO Annual Meeting

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*Exploratory long-term OS analyses of TIVO-3 continue to trend in favor of tivozanib, patients with PFS at 1 year demonstrated a 55% reduction in risk of death on tivozanib as compared to sorafenib*

*Latest analysis of Phase 2 study show tivozanib demonstrated promising activity in nccRCC patients, a difficult to treat patient population for current therapies*

*An overview of the ongoing TiNivo-2 study, evaluating tivozanib in combination with nivolumab*

BOSTON, June 06, 2022 (GLOBE NEWSWIRE) -- AVEO Oncology (Nasdaq: AVEO), a commercial stage, oncology focused biopharmaceutical company, presented three posters during the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting highlighting data for tivozanib, the Company's oral, once-daily next-generation vascular endothelial growth factor receptor (VEGFR) tyrosine kinase inhibitor (TKI) designed to block the VEGF pathway by potently and selectively inhibiting all three VEGF receptors.

Michael Bailey, president and chief executive officer of AVEO, stated, "We are pleased to present these three posters at this year's ASCO Annual Meeting, which we believe further showcase the profile of tivozanib as an effective therapy for relapsed or refractory advanced (R/R) renal cell carcinoma (RCC) patients. The overall survival (OS) data from TIVO-3 continue to improve with long-term follow up, including a significant 55% reduction in death with the subset of patients with greater than one year progression free survival (PFS). In addition, we've highlighted an analysis of a Phase 2 study which shows tivozanib demonstrated promising activity in non-clear cell renal cell carcinoma (nccRCC) patients, a difficult to treat patient population. A third poster presented at the ASCO Annual Meeting showcases our most advanced clinical combination initiative — our ongoing Phase 3 TiNivo-2 clinical trial evaluating tivozanib in combination with nivolumab — which is designed to generate data to support regulatory approval of tivozanib combined with nivolumab in the larger second-line R/R RCC market following prior immune checkpoint inhibitor therapy."

**Poster title: "Maturation of overall survival (OS) in TIVO-3 with long-term follow-up." - (Abstract: 4557; Poster: 48)**

AVEO presented a poster evaluating OS with extended mean follow-up. As previously announced, at two years following the last patient in the TIVO-3 study, the mean follow-up was 17.9 months (data cutoff was August 2019) and 65% of patients experienced an event, with an OS hazard ratio (HR) of 0.99 (95% CI 0.76–1.29). With subsequent OS analyses and mean follow-up extended to 22.8 months, the data show that 80% of patients ultimately experienced events and the hazard ratio of OS lowered to 0.89 (95% CI 0.70–1.14), trending in favor of tivozanib.

A conditional survival analysis was also performed which looked at OS for patients whose disease was progression free at the 12 month landmark, showing a statistically significant 55% relative reduction in the risk of death with tivozanib over sorafenib in this population (HR 0.45; 95% CI 0.22–0.91). The median OS for those patients achieving 12 month PFS was 48.3 months (tivozanib) as compared to 32.8 months (sorafenib), once again demonstrating the long-term benefit of tivozanib.

**Poster title: "Activity of tivozanib in non-clear cell renal cell carcinoma (nccRCC): Subgroup analysis from a phase 2 randomized discontinuation trial." - (Abstract: 4542; Poster: 33)**

AVEO presented data from a subgroup analysis of patients with nccRCC who had no prior VEGF targeted treatment in its Phase 2 randomized discontinuation trial evaluating tivozanib. These data showed that the overall response rate (ORR) at 16 weeks in all treated patients with nccRCC was 15.2% by independent radiology review. The best unconfirmed overall response rate (ORR) and confirmed ORR (at any time point) was 31.6% and 21.1%, respectively. The disease control rate was 74%. The median PFS was 6.7 months (204 days). Safety was not analyzed by histology but there were no new safety signals and this was consistent with tivozanib labelling in the intent to treat population.

The analysis concluded that tivozanib demonstrated activity and a favorable safety profile in patients with nccRCC. These data add to the body of evidence supporting VEGFR TKI use in advanced RCC, including in non-clear cell histologies.

**Trials in Progress Poster Presentation "TiNivo-2: A phase 3, randomized, controlled, multicenter, open-label study to compare tivozanib in combination with nivolumab to tivozanib monotherapy in subjects with renal cell carcinoma who have progressed following one or two lines of therapy where one line was an immune checkpoint inhibitor." - (Abstract: TPS4605; Poster: 92b)**

The Company presented a trial in progress poster for the Phase 3 TiNivo-2 trial, which is evaluating the combination of tivozanib and Bristol-Myers Squibb's OPDIVO® (nivolumab), an antibody directed against programmed death-1 (PD-1), versus tivozanib monotherapy for the treatment of RCC patients progressing following prior immune checkpoint inhibitor therapy. Subjects will receive tivozanib 1.34 mg orally once daily for 21 consecutive days followed by seven days off, on the monotherapy arm, and tivozanib 0.89 mg at the same schedule in addition to nivolumab 480 mg intravenously every four weeks on the combination arm.

The primary objective of the study is to compare the PFS of tivozanib in combination with nivolumab to monotherapy tivozanib. A sample size of 326 subjects, with 191 events will provide at least 80% power to detect a 50% improvement in PFS as assessed by IRR. Secondary endpoints include assessment of OS, ORR and duration of response, as well as safety and tolerability. Exploratory endpoints are to assess the quality of life and to

investigate the pharmacokinetics of tivozanib.

TiNivo-2 opened for enrollment during the third quarter of 2021 and currently expects to complete enrollment in the first half of 2023.

**About FOTIVDA® (tivozanib)**

FOTIVDA® (tivozanib) is an oral, next-generation vascular endothelial growth factor receptor (VEGFR) tyrosine kinase inhibitor (TKI). It is a potent, selective inhibitor of VEGFRs 1, 2, and 3 with a long half-life designed to improve efficacy and tolerability. AVEO received U.S. Food and Drug Administration (FDA) approval for FOTIVDA on March 10, 2021 for the treatment of adult patients with relapsed or refractory advanced renal cell carcinoma (RCC) following two or more prior systemic therapies. FOTIVDA was approved in August 2017 in the European Union and other countries in the territory of its partner EUSA Pharma (UK) Limited for the treatment of adult patients with advanced RCC. FOTIVDA has been shown to significantly reduce regulatory T-cell production in preclinical models.[1] FOTIVDA was discovered by Kyowa Kirin.

**INDICATIONS**

FOTIVDA is indicated for the treatment of adult patients with relapsed or refractory advanced renal cell carcinoma (RCC) following two or more prior systemic therapies.

**IMPORTANT SAFETY INFORMATION**

**WARNINGS AND PRECAUTIONS**

**Hypertension and Hypertensive Crisis:** Control blood pressure prior to initiating FOTIVDA. Monitor for hypertension and treat as needed. For persistent hypertension despite use of anti-hypertensive medications, reduce the FOTIVDA dose.

**Cardiac Failure:** Monitor for signs or symptoms of cardiac failure throughout treatment with FOTIVDA.

**Cardiac Ischemia and Arterial Thromboembolic Events:** Closely monitor patients who are at increased risk for these events. Permanently discontinue FOTIVDA for severe arterial thromboembolic events, such as myocardial infarction and stroke.

**Venous Thromboembolic Events:** Closely monitor patients who are at increased risk for these events. Permanently discontinue FOTIVDA for severe venous thromboembolic events.

**Hemorrhagic Events:** Closely monitor patients who are at risk for or who have a history of bleeding.

**Proteinuria:** Monitor throughout treatment with FOTIVDA. For moderate to severe proteinuria, reduce the dose or temporarily interrupt treatment with FOTIVDA.

**Thyroid Dysfunction:** Monitor before initiation and throughout treatment with FOTIVDA.

**Risk of Impaired Wound Healing:** Withhold FOTIVDA for at least 24 days before elective surgery. Do not administer for at least 2 weeks following major surgery and adequate wound healing. The safety of resumption of FOTIVDA after resolution of wound healing complications has not been established.

**Reversible Posterior Leukoencephalopathy Syndrome (RPLS):** Discontinue FOTIVDA if signs or symptoms of RPLS occur.

**Embryo-Fetal Toxicity:** Can cause fetal harm. Advise patients of the potential risk to a fetus and to use effective contraception.

**Allergic Reactions to Tartrazine:** The 0.89 mg capsule of FOTIVDA contains FD&C Yellow No.5 (tartrazine) which may cause allergic-type reactions (including bronchial asthma) in certain susceptible patients.

**ADVERSE REACTIONS**
The most common (≥20%) adverse reactions were fatigue, hypertension, diarrhea, decreased appetite, nausea, dysphonia, hypothyroidism, cough, and stomatitis, and the most common Grade 3 or 4 laboratory abnormalities (≥5%) were sodium decreased, lipase increased, and phosphate decreased.

**DRUG INTERACTIONS**

**Strong CYP3A4 Inducers:** Avoid coadministration of FOTIVDA with strong CYP3A4 inducers.

**USE IN SPECIFIC POPULATIONS**

**Lactation:** Advise not to breastfeed.
**Females and Males of Reproductive Potential:** Can impair fertility.
**Hepatic Impairment:** Adjust dosage in patients with moderate hepatic impairment. Avoid use in patients with severe hepatic impairment.

**To report SUSPECTED ADVERSE REACTIONS, contact AVEO Pharmaceuticals, Inc. at 1-833-FOTIVDA (1-833-368-4832) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.**

**Please see FOTIVDA Full Prescribing Information which is available at www.FOTIVDA.com.**

**About Advanced Renal Cell Carcinoma**

According to the American Cancer Society's 2021 statistics, renal cell carcinoma (RCC) is the most common type of kidney cancer, which is among the ten most common cancers in both men and women. Approximately 73,750 new cases of kidney cancer will be diagnosed annually and about 14,830 people will die from this disease. In patients with late-stage disease, the five-year survival rate is 13%. Agents that target the vascular endothelial growth factor (VEGF) pathway have shown significant antitumor activity in RCC.[2] According to a 2019 publication, 50% of the approximately 10,000 patients who progress following two or more lines of therapy choose not to receive further treatment,[3] which may be attributable

to tolerability concerns and a lack of data to support evidence-based treatment decisions in this highly relapsed or refractory patient population.

**About AVEO Pharmaceuticals, Inc.**

AVEO is a commercial stage, oncology focused biopharmaceutical company committed to delivering medicines that provide a better life for patients with cancer. AVEO currently markets FOTIVDA® (tivozanib) in the U.S. for the treatment of adult patients with relapsed or refractory advanced renal cell carcinoma (RCC) following two or more prior systemic therapies. AVEO continues to develop FOTIVDA in immuno-oncology and other novel targeted combinations in RCC and other indications, and has other investigational programs in clinical development. AVEO is committed to creating an environment of diversity, equity and inclusion to diversify representation within the company.

**Cautionary Note Regarding Forward-Looking Statements**

This press release contains forward-looking statements of AVEO within the meaning of the Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties. All statements, other than statements of historical fact, contained in this press release are forward-looking statements. The words “advance,” “aim,” “anticipate,” “believe,” “continue,” “could,” “design,” “estimate,” “expect,” “goal,” “intend,” “look forward,” “may,” “plan,” “potential,” “project,” “promising,” “seek,” “should,” “strategy,” “will,” “would,” or the negative of these terms or other similar expressions, are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include, among others, statements about: the potential efficacy, safety and tolerability of tivozanib, both as a stand-alone drug candidate and in combination with other therapies, in RCC, nccRCC and other indications; the potential that early and consistent PFS benefit with tivozanib ultimately may be associated with a trend toward improved overall survival; the potential for tivozanib to provide efficacy and safety in patients with non-clear cell histologies, such as nccRCC; the date enrollment will be completed for AVEO’s pivotal Phase 3 TiNivo-2 trial and the potential for the TiNivo-2 trial to meet its primary and secondary endpoints; AVEO’s plans, strategies and execution for current and future clinical trials and preclinical studies of tivozanib; AVEO's ability to pursue regulatory strategies based on the results of clinical trials and preclinical studies of tivozanib, including the potential for the Phase 3 TiNivo-2 trial evaluating tivozanib in combination with nivolumab to generate data to support regulatory approval of tivozanib combined with nivolumab in the larger second-line R/R RCC market following prior immune checkpoint inhibitor therapy; AVEO’s ability to commercialize tivozanib in combination with nivolumab in the larger second-line R/R RCC market following prior immune checkpoint inhibitor therapy if granted regulatory approval for the combination in that setting; and the potential commercial opportunity of tivozanib and AVEO’s other product candidates. AVEO has based its expectations and estimates on assumptions that may prove to be incorrect. As a result, readers are cautioned not to place undue reliance on these expectations and estimates. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements that AVEO makes due to a number of important factors, including risks relating to: AVEO’s ability, and the ability of its licensees and collaborators, to demonstrate to the satisfaction of applicable regulatory agencies such as the FDA the safety, efficacy, and clinically meaningful benefit of tivozanib, and risks relating to the timing and costs of seeking and obtaining regulatory approvals; AVEO’s dependence on third-party vendors for the development, manufacture, supply, storage and distribution of tivozanib; AVEO’s ability to enter into and maintain its third party collaboration and license agreements, and its ability, and the ability of its strategic partners, to achieve development and commercialization objectives under these arrangements; AVEO’s and its collaborators’ ability to successfully enroll and complete clinical trials, including the Phase 3 TiNivo-2 trial; AVEO’s ability to maintain compliance with regulatory requirements applicable to tivozanib; AVEO’s ability to obtain and maintain adequate protection for intellectual property rights relating to tivozanib; unplanned capital requirements; adverse general economic, political and industry conditions; the potential adverse effects of the COVID-19 pandemic on AVEO’s business continuity, financial condition, results of operations, liquidity and ability to commercialize FOTIVDA, manufacture clinical and commercial product and timely initiate new trials or complete its ongoing clinical trials; competitive factors; and those risks discussed in the sections titled “Risk Factor Summary,” “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Liquidity and Capital Resources” included in AVEO’s quarterly and annual reports on file with the Securities and Exchange Commission (SEC) and in other filings that AVEO makes with the SEC. The forward-looking statements in this press release represent AVEO’s views as of the date of this press release, and subsequent events and developments may cause its views to change. While AVEO may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so. You should, therefore, not rely on these forward-looking statements as representing AVEO's views as of any date other than the date of this press release.

Any reference to AVEO’s website address in this press release is intended to be an inactive textual reference only and not an active hyperlink.

**References**


1. Pawlowski N et al. AACR 2013. Poster 3971.
2. J Angulo and O Shapiro, Cancers (Basel) 2019 Sep; 11(9): 1227. [10.3390/cancers11091227]
3. Decision Resources. RCC landscape and forecast. December 12, 2019.



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