



## AVEO Oncology Announces European Urology Publication of Final Overall Survival Data from Phase 3 TIVO-3 Study of Tivozanib in Renal Cell Carcinoma

September 15, 2020

BOSTON--(BUSINESS WIRE)--Sep. 15, 2020-- AVEO Oncology (Nasdaq: AVEO) today announced that final overall survival (OS) results from its Phase 3 TIVO-3 study were published in the journal *European Urology*. TIVO-3 is the Company's pivotal Phase 3 trial comparing tivozanib, AVEO's next-generation vascular endothelial growth factor (VEGF) receptor tyrosine kinase inhibitor (TKI) drug candidate, to sorafenib in third and fourth line renal cell carcinoma (RCC). The article, titled "Final Overall Survival Results from a Phase 3 Study to Compare Tivozanib to Sorafenib as Third- or Fourth-line Therapy in Subjects with Metastatic Renal Cell Carcinoma," is available online first via [this link](#).

"TIVO-3 represents the first positive superiority study in the growing population of patients who have relapsed or become refractory to multiple lines of therapy, including checkpoint inhibitors," said Sumanta (Monty) Pal, MD, Associate Clinical Professor, Department of Medical Oncology and Therapeutics Research, and Co-director, Kidney Cancer Program, at City of Hope Comprehensive Cancer Center, and lead author. "TIVO-3 data suggest a favorable safety and efficacy profile relative to sorafenib as demonstrated by superior anti-tumor progression free survival and overall response activity vs. another VEGFR TKI, coupled with fewer dose reductions, interruptions and discontinuations. The OS hazard ratio (HR) is consistent with previous Phase 3 studies comparing two VEGF-directed agents. I believe that tivozanib has the potential to offer patients a meaningful new treatment option in a setting currently lacking an evidence-based standard of care."

"For RCC patients who have relapsed or are refractory to multiple lines of therapy, the lack of well controlled clinical data to guide treatment decisions in this advanced relapsed/refractory population poses challenges for patients and treating physicians," said Michael Bailey, president and chief executive officer of AVEO. "We expect that Tivozanib's TIVO-3 data has the potential to guide important treatment decisions in this setting and ultimately improve outcomes and patient experience. We look forward to working with the U.S. Food and Drug Administration (FDA) as they continue to review our New Drug Application (NDA) submission."

In June 2020, AVEO announced that the FDA accepted for filing its NDA seeking approval for tivozanib as a treatment for relapsed or refractory RCC. The FDA has assigned the application standard review and a Prescription Drug User Fee Act target action date of March 31, 2021. The FDA also indicated that they do not currently plan on convening an Oncologic Drug Advisory Committee (ODAC) to discuss the application. The NDA submission is based on the TIVO-3 study and is also supported by three additional trials in RCC and includes safety data from over 1,000 clinical trial subjects and several years of commercial availability in Europe.

### Results in Detail

Patients enrolled in the TIVO-3 trial (n=350) were randomized and stratified by prior regimen and IMDC prognostic score. Prior treatment regimens included prior checkpoint inhibitor and VEGF TKI therapies (n=91), two prior VEGF TKI therapies (n=159) and prior VEGF TKI and other therapies (n=100). As previously announced, the TIVO-3 trial met the primary endpoint of progression free survival (PFS), with a median PFS of 5.6 months in the tivozanib arm vs. 3.9 months in the sorafenib arm (HR=0.73; p=0.02), and the secondary endpoint of overall response rate (ORR) (18% vs. 8%; p=0.02).

For the secondary endpoint of OS, the OS HR, which assesses the overall relative risk of death, was 0.97 (95% CI: 0.75-1.24; p=0.82), favoring tivozanib and improving from the previously reported interim HR of 0.99. Median OS, representing a single point in time in the OS curve, was 16.4 months for tivozanib (95% CI: 13.4-22.2) and 19.2 months for sorafenib (95% CI: 15.0-24.2). These OS HR results are similar to those of prior VEGFR TKI vs. VEGFR TKI studies in RCC.<sup>1-4</sup>

Tivozanib was found to be generally well-tolerated, with grade 3 or higher adverse events (AEs) consistent with those observed in previous tivozanib trials. The most common AE in patients receiving tivozanib was hypertension (38% vs. 25% for sorafenib, of treated patients), an AE known to reflect effective VEGF pathway inhibition. Infrequent but severe AEs reported in greater number in the tivozanib arm were thrombotic events (5% vs. 4% for sorafenib, of treated patients) similar to those observed in previous tivozanib studies. Dose reductions and interruptions due to AEs were significantly lower for tivozanib vs. sorafenib, despite nearly double the average number of cycles initiated for the tivozanib arm (11.9 months vs. 6.7 months for sorafenib), and treatment related AEs leading to permanent discontinuation were 8% for tivozanib vs. 15% for sorafenib.

### About Tivozanib (FOTIVDA®)

Tivozanib is an oral, once-daily, next-generation vascular endothelial growth factor receptor (VEGFR) tyrosine kinase inhibitor (TKI) discovered by Kyowa Kirin and approved as FOTIVDA® for the treatment of adult patients with advanced renal cell carcinoma (RCC) in the European Union and other countries in the EUSA territory. It is a potent, selective and long half-life inhibitor of all three VEGF receptors and is designed to optimize VEGF blockade while minimizing off-target toxicities, potentially resulting in improved efficacy and minimal dose modifications.<sup>5,6</sup> Tivozanib is being studied in the TIVO-3 trial, which is supporting a regulatory submission of tivozanib in the U.S. seeking marketing approval as a treatment for relapsed or refractory RCC. Tivozanib has been shown to significantly reduce regulatory T-cell production in preclinical models<sup>7</sup> and has demonstrated synergy in combination with nivolumab (anti PD-1) in a Phase 2 study in RCC.<sup>8</sup> Tivozanib has been investigated in several tumor types, including renal cell, hepatocellular, colorectal, ovarian and breast cancers. Tivozanib is also being studied by partner Kyowa Kirin in non-oncology indications.

## About AVEO Pharmaceuticals, Inc.

AVEO is developing an oncology pipeline that is being designed to provide a better life for patients with cancer. AVEO's strategy is to focus its resources toward development and commercialization of its product candidates in North America, while leveraging partnerships to support development and commercialization in other geographies. AVEO's lead candidate, tivozanib is approved as FOTIVDA<sup>®</sup> in the European Union and other countries in the EUSA territory for the treatment of adult patients with advanced renal cell carcinoma. AVEO is working to develop and potentially commercialize tivozanib in North America as a treatment for renal cell carcinoma and hepatocellular carcinoma. AVEO has previously reported promising early clinical data on ficlatuzumab (anti-HGF mAb) in head and neck cancer, acute myeloid leukemia and pancreatic cancer and is conducting a randomized Phase 2 confirmatory clinical trial of ficlatuzumab in head and neck cancer. AVEO's earlier-stage pipeline includes several monoclonal antibodies in oncology development, including AV-203 (anti-ErbB3 mAb), AV-380 (anti-GDF15 mAb) and AV-353 (anti-Notch 3 mAb). AVEO is committed to creating an environment of diversity and inclusion as a foundation for innovation.

## 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 "anticipate," "believe," "expect," "hope," "intend," "may," "plan," "potential," "could," "should," "would," "seek," "look forward," "advance," "goal," "strategy," 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 for tivozanib as a treatment option for patients with advanced HCC or relapsed/refractory or advanced RCC; the potential efficacy, safety, and tolerability of tivozanib, both as a stand-alone drug candidate and in combination with other therapies in several indications; AVEO's execution of its clinical and regulatory strategy for tivozanib; AVEO's plans and strategies for current and future clinical trials of tivozanib, ficlatuzumab and AV-380 and for commercialization of tivozanib in the United States; and AVEO's strategy, prospects, plans and objectives for its product candidates and for the Company generally. 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: whether the results of TIVO-3 are sufficient to obtain marketing approval for tivozanib in the U.S., which turns on the ability of AVEO to demonstrate to the satisfaction of the FDA the safety and efficacy of tivozanib based upon the findings of TIVO-3, including its data with respect to PFS, the rate of adverse events, OS and other information that the FDA may consider to be relevant to an approval determination; AVEO's ability, and the ability of its licensees, to demonstrate to the satisfaction of applicable regulatory agencies such as the FDA the safety, efficacy and clinically meaningful benefit of AVEO's product candidates, including, in particular, tivozanib and ficlatuzumab; and 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 faces other risks relating to its business as well, including risks relating to the timing and costs of seeking and obtaining regulatory approval; AVEO's and its collaborators' ability to successfully enroll and complete clinical trials; AVEO's ability to maintain compliance with regulatory requirements applicable to its product candidates; AVEO's ability to obtain and maintain adequate protection for intellectual property rights relating to its product candidates; AVEO's ability to successfully implement its strategic plans, including its ability to successfully launch and commercialize tivozanib if it may be approved for commercialization by the FDA; AVEO's ability to raise the substantial additional funds required to achieve its goals, including those goals pertaining to the development and commercialization of tivozanib; unplanned capital requirements; AVEO's ability to access future borrowings under the Hercules loan facility, which turns on the achievement of milestones related to the approval and commercialization of tivozanib in the U.S., which milestones may not be achieved; adverse general economic 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 successfully and timely enroll, complete and read-out data from its clinical trials; competitive factors; and those risks discussed in the sections titled "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. Hutson et al. *Clinical Genitourinary Cancer*; Vol. 15, No. 1, 72-6
2. Choueiri et al. *European Journal of Cancer* 2018; 94: 115-125
3. Motzer et. al. *Lancet Oncol* 2013; 14: 552–62
4. Motzer, et al. *N Engl J Med*. 2014;370(18):1769-1770
5. Fotivda (Tivozanib) SmPC August 2017
6. Motzer RJ, Nosov D, Eisen T, et al. *J Clin Oncol* 2013; 31(30): 3791-9
7. Pawlowski N et al. AACR 2013. Poster 3971
8. Barthelemy et al. ESMO 2018. Poster 878P

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