



## **AVEO Oncology Announces Phase 3 TIVO-3 Trial of Tivozanib in Renal Cell Carcinoma Meets Primary Endpoint**

- *First and Only Positive Phase 3 Study in Third- and Fourth-Line RCC -*
- *Primary Endpoint Shows 44% Improvement in Median PFS and 26% Reduction in Risk of Progression or Death (HR=0.74, p=0.02) for Tivozanib Compared to Sorafenib -*
- *Data for Secondary Endpoint of Overall Survival Not Yet Mature; Final Analysis Planned for August 2019 -*
- *Goal to Submit NDA in Approximately Six Months -*
- *AVEO to Host Conference Call Today at 5:00 pm Eastern Time -*

**CAMBRIDGE, Mass. – November 5, 2018** – AVEO Oncology (NASDAQ: AVEO) today announced positive topline results from the primary analysis of the TIVO-3 trial, the Company's Phase 3 randomized, controlled, multi-center, open-label study to compare tivozanib (FOTIVDA<sup>®</sup>) to sorafenib in 351 subjects with highly refractory advanced or metastatic renal cell carcinoma (RCC).

The trial met its primary endpoint of demonstrating a statistically significant benefit in progression-free survival (PFS). Tivozanib demonstrated a 44% improvement in median PFS and 26% reduction in risk of progression or death (Hazard Ratio [HR]=0.74, p=0.02). Median PFS was 5.6 months for tivozanib compared to 3.9 months for sorafenib. The TIVO-3 trial enrolled patients with RCC who have failed at least two prior regimens. Among these, approximately 26% of patients received checkpoint inhibitor therapy in earlier lines of treatment. Tivozanib PFS was longer than sorafenib both in patients who received prior checkpoint inhibitor therapy and those who did not.

The analysis of the secondary endpoint of overall survival (OS) was not mature at the time of the final PFS analysis, with only 46% of potential OS events having been reported. At the time of the preliminary OS analysis, no statistically significant difference in OS was observed (HR=1.06, p=0.69). The final survival analysis per protocol is planned for August 2019, two years following the last patient enrolled. Detailed results of the trial will also be submitted for presentation at an upcoming major medical meeting. The secondary endpoint of overall response rate for patients receiving tivozanib was 18% compared to 8% for patients receiving sorafenib (p=0.02).

Tivozanib was generally well-tolerated, with grade 3 or higher adverse events consistent with those observed in previous tivozanib trials. Infrequent but severe adverse events reported in greater number in the tivozanib arm were thrombotic events similar to those observed in previous tivozanib studies. The most common adverse event in patients receiving tivozanib was hypertension, an adverse event known to reflect effective VEGF pathway inhibition.<sup>2</sup>

Based on results from the TIVO-3 trial, together with the previously completed Phase 3 TIVO-1 trial of tivozanib in the first line treatment of RCC, the Company's goal is to submit a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) in approximately six months.

"Tivozanib's therapeutic profile is distinct among VEGF TKIs as a treatment for RCC, with the TIVO-3 trial demonstrating a significant PFS benefit and a favorable tolerability profile," said Brian Rini, MD, Professor of Medicine, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Director, Cleveland Clinic Genitourinary Cancer Program, and principal investigator of the TIVO-3 trial. "In the advanced disease setting, these outcomes are particularly meaningful, providing the first large, pivotal dataset that shows sequencing of treatment following earlier TKI and immunotherapy treatment. This profile suggests an important place for tivozanib in the evolving treatment paradigm for RCC and, taken together with early combination data, the need to study tivozanib further in combination with immunotherapies."

"Our determination to fight for tivozanib in 2015, when AVEO faced an important strategic crossroads, came from our belief that it could have a meaningful impact not just on how a disease was treated, but also what the patient experiences through that treatment. Today's outcome is the culmination of that multi-year effort, and a first step in our goal to improve both outcomes and patient experience," said Michael Bailey, president and chief executive officer of AVEO. "We owe our deepest gratitude to the healthcare professionals, many of whom long believed in the potential of tivozanib, and to the patients and their families for participating in our pivotal studies."

### **Conference Call and Webcast**

In connection with this announcement, AVEO will host a conference call and slide webcast today, November 5, 2018 at 5:00 pm Eastern Time. The call can be accessed by dialing (844) 882-7841 (U.S. and Canada) or (574) 990-9828 (international). The passcode for the conference call is 7078805. To access the live audio webcast, or the subsequent archived recording, please visit the Investors section of the AVEO website at [www.aveooncology.com](http://www.aveooncology.com). The webcast will be recorded and available for replay on AVEO's website for two weeks.

### **About TIVO-3**

The TIVO-3 trial was designed to enroll patients with RCC who have failed at least two prior regimens, including VEGFR-TKI therapy. Eligible patients may also have received checkpoint inhibitor therapy in earlier lines of treatment. Patients are randomized 1:1 to receive either tivozanib or sorafenib, with no crossover between arms. The primary endpoint of the study is progression free survival (PFS). Secondary endpoints include overall survival (OS), overall response rate (ORR), and safety and tolerability. TIVO-3, together with the previously completed TIVO-1 trial of tivozanib in the first line treatment of RCC, is designed to support a regulatory submission of tivozanib in the U.S. as a treatment for RCC in multiple lines of therapy. TIVO-3 patients were exclusively enrolled in North America, Western Europe, and Central Europe.

### **About Tivozanib (FOTIVDA<sup>®</sup>)**

Tivozanib (FOTIVDA<sup>®</sup>) is an oral, once-daily, vascular endothelial growth factor (VEGF) tyrosine kinase inhibitor (TKI) discovered by Kyowa Hakko Kirin and approved for the treatment

of adult patients with advanced renal cell carcinoma (RCC) in the European Union plus Norway and Iceland. 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>3,4</sup> Tivozanib has been shown to significantly reduce regulatory T-cell production in preclinical models, enabling potentially enhanced activity when used in combination with immune modulating therapy.<sup>5</sup> Tivozanib has been investigated in several tumors types, including renal cell, hepatocellular, colorectal and breast cancers.

## **About AVEO**

AVEO Pharmaceuticals, Inc. (the “Company”) is a biopharmaceutical company dedicated to advancing a broad portfolio of targeted medicines for oncology and other areas of unmet medical need. The Company’s strategy is to retain North American rights to its oncology portfolio while securing partners in development and commercialization outside of North America. The Company is seeking to develop and commercialize its lead candidate tivozanib in North America as a treatment for advanced or metastatic renal cell carcinoma (“RCC”). The Company has outlicensed tivozanib (FOTIVDA®) for oncology in Europe and other territories outside of North America. Tivozanib is approved in the European Union, as well as Norway and Iceland, for the first-line treatment of adult patients with RCC and for adult patients who are vascular endothelial growth factor receptor and mTOR pathway inhibitor-naïve following disease progression after one prior treatment with cytokine therapy for RCC. The Company has entered into partnerships for the development and commercialization of AV-203 (CAN017) and ficlatuzumab, both clinical stage assets in oncology. The Company is currently seeking a partner to develop the AV-353 platform, a preclinical asset, worldwide for the potential treatment of pulmonary arterial hypertension. The Company has recently regained the rights to its AV-380 program for the potential treatment of cachexia and is considering a variety of options to advance the program’s development.

For more information, please visit the Company’s website at [www.aveooncology.com](http://www.aveooncology.com).

## **Cautionary Note Regarding Forward-Looking Statements**

This press release contains forward-looking statements of AVEO 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,” “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 Company’s plans to submit an NDA to the FDA, with the goal of making such submission within approximately six months; the Company’s plan to provide final OS data in the third quarter of 2019; the expected therapeutic benefits and side effect profile of tivozanib; the Company’s plans and strategies for commercialization of tivozanib in the United States and Europe; the potential for tivozanib to have clinical potential in immunotherapy combinations; the Company’s plan to seek a partner to develop the AV-353 platform; the Company’s plans regarding AV-380 and AVEO’s strategy, prospects, plans and objectives. 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 to enter into and maintain its third party collaboration and license agreements, and its ability, and the ability of its collaborators, licensees and other strategic partners, to achieve development and commercialization objectives under these arrangements; and 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 tivozanib. AVEO faces other risks relating to its business as well, including risks relating to its ability to file an NDA for tivozanib in the time frame it currently estimates; its and its collaborators' ability to successfully enroll and complete clinical trials, including the TIVO-3 and TiNivo studies; AVEO's ability to achieve and maintain compliance with all 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 and technologies; AVEO's ability to successfully implement its strategic plans; 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; adverse general economic and industry conditions; competitive factors; and those risks discussed in the section 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 may make with the SEC in the future. The forward-looking statements in this press release represent AVEO's views as of the date of this press release. AVEO anticipates that 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

- <sup>1</sup>. Wong M, et al, J Med Econ 2012, 28 1-10
- <sup>2</sup>. Robinson E et al. Semin Nephrol. 2010 Nov; 30(6): 591–601.
- <sup>3</sup>. Fotivda (Tivozanib) SmPC August 2017
- <sup>4</sup>. Motzer RJ, Nosov D, Eisen T, et al. J Clin Oncol 2013; 31(30): 3791-9.
- <sup>5</sup>. Pawlowski N et al. AACR 2013. Poster 3971.

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