



## **AVEO Oncology Announces Regulatory Update for Tivozanib in Renal Cell Carcinoma**

November 4, 2019

*- NDA Filing Planned for 1Q20 for Relapsed/Refractory RCC –*

*- Company Plans Final OS Analysis in 2Q20 -*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Nov. 4, 2019-- AVEO Oncology (NASDAQ: AVEO) today provided a regulatory update following a meeting with the U.S. Food and Drug Administration (FDA) to discuss results from the August 2019 overall survival (OS) analysis of the TIVO-3 trial and the Company's proposal to proceed with a New Drug Application (NDA) for tivozanib.

TIVO-3 is the Company's Phase 3 randomized, controlled, multi-center, open-label study to compare tivozanib, the Company's vascular endothelial growth factor receptor tyrosine kinase inhibitor (VEGFR-TKI), to sorafenib in 350 subjects with highly refractory metastatic renal cell carcinoma (RCC). The TIVO-3 trial was designed to address the FDA's concerns regarding the OS trend in the TIVO-1 trial. In the TIVO-1 trial, the Company's initial RCC pivotal trial, the FDA found that the inconsistent progression free survival (PFS) and OS results and imbalance in post study treatments made the trial results uninterpretable and inconclusive when making a risk-benefit assessment necessary for drug approval.

The Company previously announced that the TIVO-3 trial met its primary endpoint of demonstrating a significant improvement in PFS. The study also demonstrated a significant improvement in the secondary endpoint of overall response rate. The August 2019 analysis of the secondary endpoint of OS was the second prespecified interim OS analysis of the TIVO-3 trial, and showed an updated OS hazard ratio (HR) of 0.99 at two years from the last patient enrolled in the study.

In the FDA's preliminary feedback, based on its assessment of the totality of evidence presented to date, the FDA recommended that the Company not submit an NDA at this time. The FDA stated that it remained concerned about the results of TIVO-3 in the context of the overall development of tivozanib. The FDA noted that the Company's current interim OS results do not abrogate the FDA's concerns over detriment and that those results may worsen with final analysis at 263 events, and that the median OS for tivozanib is worse than that of sorafenib.

In view of the changing first-line treatment landscape as well as the FDA's continued concerns, the Company informed the FDA that it intends to narrow its proposed indication to relapsed/refractory RCC. At the meeting, the FDA acknowledged AVEO's responses and reiterated its concerns about the survival information and the totality of data. The FDA noted that the choice to submit the data is the Company's, and that a discussion with the Oncologic Drug Advisory Committee will likely be required. The FDA said that if AVEO wishes to proceed with a revised OS analysis in June 2020, AVEO should submit an updated statistical analysis plan (SAP) with a planned OS update based on the projected number of events at that time.

AVEO intends to submit to the FDA an update to the SAP for the final OS analysis consistent with these discussions, followed by an NDA submission in the first quarter of 2020. AVEO expects to report the final OS analysis in June 2020 based on a May 1, 2020 cutoff, at which point the Company estimates that the study will have reached approximately 263 OS events, as discussed with the FDA. The FDA and the Company agreed that if the final analysis yields an OS HR above 1.00, the Company will withdraw its NDA application.

"During the meeting with the FDA, we believe that we established an appropriate path forward toward filing an NDA for tivozanib in the near term and a final analysis plan for OS," said Michael Bailey, president and chief executive officer of AVEO. "The continued separation of the PFS curves and the positive trend in OS HR observed from the first to the second interim analysis, together with tenfold more patients remaining progression free and on tivozanib vs. sorafenib therapy, make us believe that the final OS results will not worsen."

### **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 were 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**

Tivozanib (FOTIVDA<sup>®</sup>) is an oral vascular endothelial growth factor (VEGF) tyrosine kinase inhibitor (TKI) discovered by Kyowa Kirin and approved for the treatment of adult patients with advanced renal cell carcinoma (RCC) in the European Union plus Norway, New Zealand 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>1,2</sup> Tivozanib has been shown to significantly reduce regulatory T-cell production in preclinical models<sup>3</sup> and has demonstrated synergy in combination with nivolumab (anti PD-1) in a Phase 2 study in RCC<sup>4</sup>. Tivozanib has been investigated in several tumor types, including renal cell, hepatocellular, colorectal, ovarian and breast cancers.

### **About AVEO**

AVEO Pharmaceuticals is a biopharmaceutical company seeking to advance targeted medicines for oncology and other unmet medical needs. The Company's lead candidate is tivozanib, a potent, selective, long half-life inhibitor of vascular endothelial growth factor 1, 2 and 3 receptors, which AVEO is working to develop and commercialize in North America as a treatment for renal cell carcinoma (RCC), hepatocellular carcinoma (HCC) and other cancers. Tivozanib (FOTIVDA<sup>®</sup>) is approved by the European Commission for the treatment of adult patients with advanced RCC in the European Union plus Norway, New Zealand, and Iceland. AVEO is leveraging or seeks to leverage partnerships to develop and commercialize its pipeline of products and product candidates, including tivozanib in oncology and other indications in various geographies, and ficlatuzumab (HGF MAb) in head and neck cancer, pancreatic cancer and acute myeloid leukemia. AVEO's earlier-stage pipeline includes AV-203 (anti-ErbB3 MAb), AV-380 (GDF15 MAb) and AV-353 (Notch 3 MAb) for various oncology indications.

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 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," "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 for tivozanib, including the submission of an updated SAP and additional data to the FDA; the potential for tivozanib as a treatment option for patients with relapsed/refractory or advanced RCC; the advancement of AVEO's pipeline; the potential efficacy, safety, and tolerability of tivozanib, as a single agent and in combination with other therapies in several indications, such as RCC and HCC, including without limitation AVEO's expectations regarding the potential of tivozanib to successfully meet endpoints in the TIVO-3 trial in RCC; AVEO's plans and strategies for commercialization of tivozanib in the United States and Europe; 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: 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; AVEO's ability to successfully file an NDA for tivozanib; 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; 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 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. Fotivda (Tivozanib) SmPC August 2017.
2. Motzer RJ, Nosov D, Eisen T, et al. J Clin Oncol 2013; 31(30): 3791-9.
3. Pawlowski N et al. AACR 2013. Poster 3971.
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