



AVEO Oncology Announces FOTIVDA® (tivozanib) Approved in the European Union for the Treatment of Advanced Renal Cell Carcinoma

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CAMBRIDGE, Mass.--(BUSINESS WIRE)--Aug. 28, 2017-- AVEO Oncology (NASDAQ: AVEO) today announced that the European Commission (EC) has approved FOTIVDA® (tivozanib) for the treatment of adult patients with advanced renal cell carcinoma (RCC) in the European Union plus Norway and Iceland. Tivozanib is indicated for the first line treatment of adult patients with advanced RCC and for adult patients who are vascular endothelial growth factor receptor (VEGFR) and mTOR pathway inhibitor-naïve following disease progression after one prior treatment with cytokine therapy for advanced RCC.ⁱ EUSA Pharma, a specialty pharmaceutical company with a focus on oncology and oncology supportive care, is the European licensee for tivozanib. Tivozanib is an oral, once-daily, potent and highly-selective vascular endothelial growth factor receptor tyrosine kinase inhibitor (VEGFR-TKI).

Dr. Bernard Escudier, Medical Oncologist and member of the Genitourinary Tumour Board of Gustave Roussy, France, commented "This is excellent news for patients with metastatic RCC. Outcomes in this disease have greatly improved with the introduction of targeted therapies, meaning that patients are living for longer. However, we are still in need of effective and well tolerated new treatments in metastatic RCC and thus, tivozanib is a welcomed addition."

The approval from the EC follows the recommendation from the Committee for Medical Products for Human Use (CHMP).ⁱⁱ The decision was primarily based on data from a global, open-label, randomized, multi-center Phase 3 trial (TIVO-1),ⁱⁱⁱ which evaluated the efficacy and tolerability of tivozanib compared to a currently available comparator VEGFR-TKI treatment (sorafenib) in 517 patients with advanced RCC. Patients treated with tivozanib experienced superior PFS (11.9 vs. 9.1 months in the overall population [HR, 0.797; 95% CI, 0.639 to 0.993; P =.042] and 12.7 vs. 9.1 months in treatment naïve patients [HR, 0.756; 95% CI, 0.580 to 0.985; P =.037]) versus sorafenib.ⁱⁱⁱ There was also an improved side effect profile with tivozanib, with only 14% (versus 43% with sorafenib) requiring a dose reduction due to adverse events (AEs). In addition, fewer people on tivozanib experienced burdensome side effects, such as diarrhea (23% vs 33%) and hand-foot syndrome (14% vs 54%).ⁱⁱⁱ

EUSA Pharma has indicated that it intends to now work with the necessary health authorities to make tivozanib available to advanced RCC patients across Europe as quickly as possible.

"The European Commission's decision is the first regulatory approval of tivozanib globally, and a tremendous accomplishment for AVEO and its partner, EUSA Pharma. We are very pleased that tivozanib is now available to patients in Europe," said Michael Bailey, president and chief executive officer of AVEO. "We also continue to make progress on the next two pillars in our tivozanib strategy: U.S. registration, driven by the pivotal Phase 3 TIVO-3 trial, which is expected to read out in the first quarter of 2018; and immunotherapy combination trials, starting with the TiNivo trial, our Opdivo® combination trial. European approval further strengthens our balance sheet by triggering an R&D payment to AVEO and provides AVEO the opportunity to achieve multiple potential commercial milestone payments, as well as royalty payments on sales, that would support our execution of the tivozanib strategy."

Under the terms of their December 2015 agreement, EUSA Pharma has agreed to pay AVEO up to \$394 million in future milestone payments and research and development funding, assuming successful achievement of specified development, regulatory and commercialization objectives. In addition, a tiered royalty will be due to AVEO ranging from a low double-digit up to mid-twenty percent on net sales of tivozanib in the agreement's territories. European marketing approval for tivozanib triggers a \$4 million research and development payment from EUSA, and AVEO will also be eligible for up to \$12 million in additional milestones from EUSA based on reimbursement and regulatory approvals. In the territories licensed to EUSA, thirty percent of milestone and royalty payments received by AVEO, excluding research and development funding, are due to Kyowa HAKKO Kirin (KHK) as a sublicensing fee. In the territories retained by AVEO, the royalty obligation to KHK ranges from the low- to mid-teens on net sales.

About RCC in Europe

RCC is the most common form of kidney cancer,^{iv} which accounts for an estimated 49,000 deaths in Europe each year.^v It is expected to be one of the fastest increasing cancers over the next ten years.^{vi} Tyrosine Kinase Inhibitor (TKI) vascular endothelial growth factor (VEGF) inhibitors are the standard of care treatment for advanced RCC in Europe, however, patients on current treatments can often experience significant side effects.^{iii,vii}

About Tivozanib (FOTIVDA®)

Tivozanib (FOTIVDA®) 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 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. Tivozanib has been investigated in several tumors types, including renal cell, colorectal and breast cancers.

About AVEO

AVEO Oncology (AVEO) is a biopharmaceutical company dedicated to advancing a broad portfolio of targeted therapeutics for oncology and other areas of unmet medical need. The Company is focused on seeking to develop and commercialize its lead candidate tivozanib, a potent, selective, long half-life inhibitor of vascular endothelial growth factor 1, 2 and 3 receptors, in North America as a treatment for renal cell carcinoma and other cancers. AVEO is leveraging multiple partnerships aimed at developing and commercializing tivozanib in oncology indications outside of North America, and at progressing its pipeline of novel therapeutic candidates in cancer and cachexia (wasting syndrome). Tivozanib (FOTIVDA®) is approved by the European Commission for the treatment of adult patients with advanced renal cell carcinoma (RCC) in the European Union plus Norway and Iceland. For more information, please visit the company's website at 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 anticipated readout of TIVO-3 in the first quarter of 2018; expectations about the potential for additional payments by EUSA Pharma; plans to progress pipeline programs; the expected benefits of tivozanib; and AVEO's strategy, prospects, plans and objectives, including as they pertain specifically to tivozanib. 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 agreements, and its ability, and the ability of its licensees and other partners, to achieve development and commercialization objectives under these arrangements; AVEO's ability, and the ability of its licensees, to demonstrate to the satisfaction of applicable regulatory agencies the safety, efficacy and clinically meaningful benefit of AVEO's product candidates, including without limitation risks relating to the ability of EUSA to successfully obtain reimbursement approval of tivozanib in the countries within its territory. AVEO faces other risks relating to its business as well, including risks relating to its 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; developments, expenses and outcomes related to AVEO's ongoing shareholder litigation; 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 Annual Report on Form 10-K for the year ended December 31, 2016, its quarterly reports on Form 10-Q 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.

ⁱ http://ec.europa.eu/health/documents/community-register/index_en.htm

ⁱⁱ CHMP summary of opinion. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Summary_of_opinion_-_Initial_authorisation/human/004131/WC500229916.pdf

ⁱⁱⁱ Motzer R.J.; Nosov D et al. Tivozanib Versus Sorafenib As Initial Targeted Therapy for Patients With Metastatic Renal Cell Carcinoma: Results From a Phase III Trial. *Journal of Clinical Oncology*. Volume 31. 2013: 30:3791

^{iv} Cancer Research UK. Kidney Cancer, Types and Grades. Available at: <http://www.cancerresearchuk.org/about-cancer/kidney-cancer/stages-types-grades/types-grades>. Last accessed May 2017.

^v Cancer Research UK. Kidney Cancer Statistics. Available at: <http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/kidney-cancer/mortality#heading-Five>. Last accessed May 2017.

^{vi} Cancer Research UK. Kidney cancer rates are increasing, so what's fuelling the surge? Available at: <http://scienceblog.cancerresearchuk.org/2017/04/24/kidney-cancer-rates-are-increasing-so-whats-fuelling-the-surge/>. Last accessed May 2017.

^{vii} Wong MKK, Mohamed AF et al. Selecting renal cell carcinoma therapy: Ranking of patient perspective on toxicities. *J Clin Oncol* 30: 303s, 2012 (suppl; abstr 4608)

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