AVEO Oncology, an LG Chem company, Present TiNivo-2 Results and TIVO-3 Exploratory Post Immunotherapy Survival Analysis at ESMO 2024

– TiNivo-2 results published in The Lancet –

– TiNivo-2 FOTIVDA® (tivozanib) monotherapy (control arm) results provide clinically meaningful efficacy and safety data following front-line immune checkpoint inhibitor (ICI) combinations –

– TIVO-3 Exploratory Overall Survival (OS) Analysis Provides Additional Data for FOTIVDA Following Immunotherapy –

– Safety results support the well-established safety profile of FOTIVDA–

BOSTON, September16, 2024 (PR Newswire) — AVEO Oncology, an LG Chem company ("AVEO"), announced today that the TiNivo-2 Phase 3 clinical trial results in patients with advanced metastatic renal cell carcinoma (RCC) whose tumors had progressed following prior ICI treatment were presented at the 2024 European Society of Medical Oncology (ESMO) congress September 13-17 in Barcelona, Spain. Additionally, a follow up exploratory analysis from TIVO-3, FOTIVDA's pivotal trial, was also presented during the conference.

The TiNivo-2 clinical trial was designed to evaluate the treatment of FOTIVDA, a vascular endothelial growth factor receptor (VEGFR) tyrosine kinase inhibitor (TKI), in combination with nivolumab, a PD-1 inhibitor, versus FOTIVDA as a single agent therapy to investigate the benefit of ICI challenge in a relapsed refractory setting.

Toni Choueiri, M.D., Director of the Lank Center for Genitourinary Oncology, Director of the Kidney Cancer Center at Dana-Farber Cancer Institute, Jerome and Nancy Kohlberg Chair and Professor of Medicine at Harvard Medical School, and lead investigator presented the first analysis of the TiNivo-2 study results at ESMO. The addition of nivolumab to FOTIVDA (0.89 mg) following prior immunotherapy did not enhance efficacy over FOTIVDA (1.34 mg) alone (hazard ratio 1.10 [95% confidence interval, 0.84-1.43; P=0.49]); as such the study did not meet its primary endpoint. In pre-planned analyses of the FOTIVDA control arm, a 9.2 month median progression free survival (PFS) was observed for patients that received FOTIVDA monotherapy as second line and for patients immediately following ICI combination therapy; the experimental arm (nivolumab plus tivozanib) had a 7.3 month median PFS in the second line and a 7.4 month median PFS for patients immediately following ICI combination therapy.

The TiNivo-2 study results add to the existing body of data in RCC suggesting there is no clinical benefit derived from rechallenging patients with immunotherapy beyond progression on previous ICIs.

“We are truly grateful for the patients who participated in TiNivo-2 so that we can continue to make evidence-based advancements in RCC treatment and patient care,” says Michael P. Bailey, AVEO Oncology Chief Executive Officer and President. “We are excited to share the comprehensive TiNivo-2 dataset with the oncology community; these data provide additional support on the use of FOTIVDA as an option in the second line following frontline immunotherapy combination treatment.”

Dr. Choueiri comments, “The PFS results in the intent-to-treat population demonstrate the activity of tivozanib in the 2nd and 3rd lines following front line immunotherapy. The safety results were also consistent with the safety profile observed in TIVO-3.”

In conjunction with the scientific presentation, the TiNivo-2 data were simultaneously published in the prestigious journal, *The Lancet*.

In addition to the TiNivo-2 data presentation, an exploratory long-term follow up analysis from the TIVO-3 study was presented by Dr. Miguel Zugman of the City of Hope Comprehensive Cancer Center at ESMO 2024. Although the post hoc analysis did not reach statistical significance, the data indicates that tivozanib trended toward improved OS compared to sorafenib, in the subset of patients previously treated with checkpoint inhibitors. The OS hazard ratio in the checkpoint inhibitor-treated subset was 0.69 (95% confidence interval, 0.43-1.11) favoring tivozanib.

TiNivo-2 Clinical Trial Details
Phase 3 clinical trial designed to evaluate the safety and efficacy of tivozanib in combination with nivolumab, as compared to tivozanib as a monotherapy, in RCC patients whose tumors have progressed following prior ICI therapy.

TIVO-3 Clinical Trial Details
TIVO-3 was a Phase 3, global, open-label, parallel-arm study comparing the safety and efficacy of FOTIVDA versus sorafenib in patients with relapsed refractory advanced RCC whose disease progressed with two or three prior systemic regimens including at least one VEGFR TKI.

About FOTIVDA
FOTIVDA is an oral, next-generation VEGFR 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 RCC following two or more prior systemic therapies, based on data from the TIVO-3 trial comparing FOTIVDA to sorafenib. FOTIVDA was approved in August 2017 in the European Union and other countries in the territory of its partner Recordati UK Ltd. for the treatment of adult patients with advanced RCC. FOTIVDA was discovered by Kyowa Kirin.

IMPORTANT SAFETY INFORMATION
WARNINGS AND PRECAUTIONS

Hypertension was reported in 45% of patients (22% ≥ Grade 3). **Hypertensive crises** were reported in 0.8% of patients. Do not initiate FOTIVDA in patients with uncontrolled hypertension. Monitor for hypertension and treat as needed. Reduce the FOTIVDA dose for persistent hypertension not controlled by anti-hypertensive medications. Discontinue FOTIVDA for severe hypertension that cannot be controlled with anti-hypertensive therapy or for hypertensive crisis.

Cardiac failures were reported in 1.6% of patients (1% ≥ Grade 3); 0.6% of events were fatal. Monitor for signs or symptoms of cardiac failure during treatment with FOTIVDA. Manage with dose interruption, dose reduction, or discontinuation.

Cardiac ischemia were reported in 3.2% of patients; 0.4% of events were fatal. **Arterial thromboembolic events** were reported in 2.0% of patients, including death due to ischemic stroke (0.1%). Closely monitor patients at risk for, or who have a history of these events. Discontinue FOTIVDA in patients who develop severe arterial thromboembolic events, such as myocardial infarction and stroke.

Venous Thrombotic Events (VTE) were reported in 2.4% of patients, including 0.3% fatal events. Closely monitor patients who are at increased risk for these events. Discontinue in patients who develop serious VTEs.

Hemorrhagic Events were reported in 11% of patients; 0.2% of events were fatal. Use FOTIVDA with caution in patients who are at risk for or who have a history of bleeding.

Proteinuria was reported in 8% of patients (2% = Grade 3). Monitor during treatment with FOTIVDA. For moderate to severe proteinuria, reduce the dose or interrupt treatment. Discontinue in patients who develop nephrotic syndrome.

Gastrointestinal (GI) Perforation including fatal cases, has been reported in patients receiving FOTIVDA. Monitor for symptoms of GI perforation or **fistula formation** periodically throughout treatment with FOTIVDA. Permanently discontinue FOTIVDA in patients who develop severe or life-threatening GI perforation.

Thyroid Dysfunction events were reported in 11% of patients (0.3% ≥ Grade 3). Monitor thyroid function before and during treatment with FOTIVDA.

Wound Healing Complications: Withhold FOTIVDA for at least 24 days prior to elective surgery and do not administer for at least 2 weeks after major surgery and until adequate wound healing is observed.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS) can occur with FOTIVDA. Evaluate for RPLS in patients presenting with seizures, headache, visual disturbances, confusion, or altered mental function. Discontinue if signs or symptoms of RPLS occur.

Embryo-fetal Toxicity: FOTIVDA can cause fetal harm. Advise patients of the potential risk to a fetus, to avoid becoming pregnant and to use contraception during treatment and for one month

after the last dose of FOTIVDA. Advise males with female partners of reproductive potential to use effective contraception during treatment and for one month after the last dose of FOTIVDA.

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

ADVERSE REACTIONS

Common adverse reactions include fatigue/asthenia, hypertension, diarrhea, decreased appetite, nausea, dysphonia, hypothyroidism, cough, and stomatitis.

Serious adverse reactions include bleeding (3.5%), venous thromboembolism (3.5%), arterial thromboembolism (2.9%), acute kidney injury (2.3%), and hepatobiliary disorders (2.3%).

DRUG INTERACTIONS

Avoid coadministration with strong CYP3A4 inducers.

USE IN SPECIFIC POPULATIONS

Advise women not to breastfeed during treatment and for at least 1 month after the last dose.

The recommended dosage for patients with end-stage renal disease has not been established.

Reduce the FOTIVDA dose for patients with moderate hepatic impairment. The recommended dosage in patients with severe hepatic impairment has not been established.

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 full Prescribing Information for FOTIVDA® (tivozanib).

About AVEO Pharmaceuticals, Inc.
AVEO is an oncology-focused biopharmaceutical company committed to delivering medicines that provide a better life for patients with cancer. AVEO currently markets FOTIVDA in the U.S. for the treatment of adult patients with relapsed or refractory advanced 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 became a wholly owned subsidiary of LG Chem Life Sciences USA, Inc. on January 19, 2023. AVEO continues to operate under the AVEO Oncology, an LG Chem company, name.

About LG Chem, Ltd. and LG Chem Life Sciences
LG Chem, Ltd. (LG Chem) is a leading global chemical company with a diversified business portfolio in the key areas of petrochemicals, advanced materials, and life sciences. The company manufactures a wide range of products from high-value added petrochemicals to renewable plastics, specializing in cutting-edge electronic and battery materials, as well as drugs and vaccines to deliver differentiated solutions for its customers. LG Chem Life Sciences develops, manufactures, and globally commercializes pharmaceutical products, with a focus on Oncology, Immunology, and Metabolic diseases. Our mission is to transform people's lives through inspiring science and leading innovation. For more information, please visit **www.lgchem.com**.

References

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2. FOTIVDA (tivozanib)[https://www.fotivda.com/fotivdapi.pdf].Boston, MA: AVEO Pharmaceuticals, Inc.

3. OPDIVO (nivolumab)[https://packageinserts.bms.com/pi/pi_opdivo.pdf].Princeton, NJ: Bristol-Myers Squibb Company.

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